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Contents

The Proteins Synthesized in Tissue Infected with Tobacco Mosaic Virus: <i>Barry Commoner et al.</i>	529
Birmingham Conference on Nuclear Physics: <i>Ernst Bleuler</i>	534
The Effect of Exposure to the Atomic Bombs on Pregnancy Termination in Hiroshima and Nagasaki: <i>J. V. Neel et al.</i>	537

News and Notes

Meeting of the American Chemical Society: <i>Walter J. Murphy</i>	541
The Effects of Allithiamine on Some Thiamine-Requiring Organisms: <i>V. G. Lilly, H. L. Barnett, and B. G. Anderson</i>	548
The Effect of Cortisone upon the Therapeutic Efficacy of Antibiotics: <i>Ernest Jancetz and Elizabeth R. Merrill</i>	549
Resumption of Heartbeat in the Rabbit Embryo after Exposure to Low Temperatures: <i>M. C. Chang</i>	550
Lack of Protective Effect of Allyl Thiourea Against X-Irradiation: <i>Robert N. Feinstein and Gladys J. Cotter</i>	552
Photoperiodic Behavior of Medium-Early Varieties of Rice: <i>Gadadhar Misra</i>	552
The Effect of ATP on the Cilia of the Pharyngeal Mucosa of the Frog: <i>Elaine F. Vorhaus and Ingrith J. Deyrup</i>	553
Evidence that Molybdenum Is a Nondialyzable Component of Xanthine Oxidase: <i>John R. Totter et al.</i>	555
Intracellular Localization of Labeled Nucleic Acid Determined with Autoradiographs: <i>J. Herbert Taylor</i>	555
Gastric Ascorbic Acid in the Gastritic Guinea Pig: <i>A. W. Breidenbach and F. E. Ray</i>	557
Chromosomal Interchanges as a Basis for the Delimitation of Species in <i>Oenothera</i> : <i>Adolph Hecht and S. L. Tandon</i>	557
Protein Metabolism and Interactions: <i>Robert L. Evans and Donald S. Amatzio</i>	558
Phospho-Di-Anhydride Formula and Relation to Nucleic Acids Structure: <i>E. Ronwin</i> ; Comment on the Discussion of Genetics by Pope Pius XII: <i>Th. Dobzhansky</i> ; Jugular Technique for Repeated Bleeding of Small Animals: <i>R. Kassel and S. Levitan</i> ; Sperm Survival in Rodents: <i>Boris B. Rubenstein</i>	560

Book Reviews: *The Human Senses*; *Starch*; *Psychiatric Dictionary* 564

Scientific Book Register 566

Handbook of Biological Data 3

Publications Received 16

Meetings & Conferences 18

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Handbook of Biological Data

THE American Institute of Biological Sciences, associated with the Division of Biology and Agriculture of the National Academy of Sciences-National Research Council, is, through its Handbook Committee, preparing a *Handbook of Biological Data*. The book is intended to serve the biologist in much the same manner that the *Handbook of Chemistry and Physics* and the *Handbook of Chemistry* serve the physical scientist.

The purpose of the *Handbook* is to present basic tabular data, both quantitative and descriptive, in the various biological sciences for easy reference by students, teachers, practitioners, and research workers. Although the book is primarily intended for biologists who are seeking information outside their field of specialization, the tables represent authoritatively evaluated data of the highest reliability available in the field.

At the present time the book is being prepared in fascicles, or sections, the first of which, "Standard Values in Blood," has been published by the Air Force as a Technical Report and also by the W. B. Saunders Company (1952). All royalties are set aside for future revisions. This section has met with enthusiastic acclaim. It is expected that the second fascicle, "Standard Values in Nutrition and Metabolism," will be published before the end of this year. This section will contain tables on daily nutrient allowances for man and farm animals that represent the latest revisions of the recommendations of the National Research Council; these revisions will probably not be published by the NRC until 1954, but permission has been obtained to have them appear in the *Handbook* prior to that time. Similar tables will be published for laboratory vertebrates and other animal forms, along with diets that supply the nutrients recommended. There will be data on: basic nutrient requirements and utilization,

covering many plant forms; diagrams representing pathways of metabolism; culture media for plants, bacteria, fungi, and algae; metabolic end products; and data on energy metabolism.

Preliminary drafts of two other fascicles, "Standard Values in Growth, Reproduction and Life Histories" and "Standard Values in Performances" (animal and plant physiology), have been completed, and it is hoped that both of these will be in print before the end of 1954. Work is also in progress on a fascicle on biochemical composition. It is planned that within the next two years the first four or five fascicles will be condensed and combined into a one-volume handbook, which will also include data drawn from other fields of biology.

It is the policy of the *Handbook* to present only what is established fact and avoid the borderline or questionable. Data to be presented are contributed by experts in the various fields of biology, and the tables are assembled by the editorial staff of the *Handbook*. Each table is then reviewed and authenticated by other experts in the field. The objective is that each value and each statement published shall represent the consensus of expert judgment in the domain of the table. The quantitative data are supplemented, in many cases, with footnotes or headnotes, or both. The contents are indexed and contain an extensive bibliography which employs a special coordinate system that identifies the contributor for each value, and its source in the literature.

Thousands of scientists in this country and all over the world have given most generously of their time as advisors, contributors, and reviewers. It is the belief of the Committee that the fascicles and final *Handbook* will justify the efforts of the many individuals who have cooperated so unselfishly toward the success of the project.

T. C. BYERLY

Chairman, The Handbook Committee

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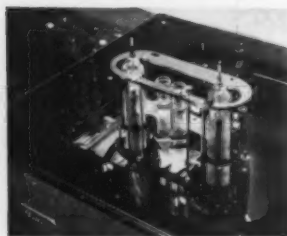
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The Proteins Synthesized in Tissue Infected with Tobacco Mosaic Virus¹

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WHEN tobacco mosaic virus (TMV) enters a suitable host cell, a new path of protein synthesis becomes established. Since one product of this pathway is a nucleoprotein identical with the inoculum, this event leads to reduplication of the virus. Biochemical characterization of the new metabolic pattern is an essential step toward understanding the mechanism of virus reduplication.

Recent investigations of this problem have shown that the initial source of nitrogen for TMV synthesis is the free ammonia present in the host tissue, and that nitrogen finally appearing in virus protein is first incorporated into an insoluble cell protein (1). These observations link the initial stages of TMV synthesis to the final product, but do not describe the intervening steps. The present paper summarizes results which serve to fill this gap in part. Reported are investigations which show that TMV biosynthesis is accompanied by the formation *de novo* of three other specific proteins and that the latter, while biologically inactive, are close immunochemical relatives of TMV. Analysis of the relationship between TMV synthesis and the synthesis of the nonvirus proteins outlines some of the steps which may be involved in TMV reduplication.

Since description of the products is often a useful way to characterize the productive apparatus, an effort was made to determine the number and nature of the new proteins synthesized in infected tissue as a result of inoculation with TMV.

The total soluble (i.e., in pH 7.0 phosphate buffer) protein complement of infected tobacco leaf was exhaustively fractionated and compared with the proteins found in otherwise identical uninfected leaf. Figure 1 shows the electrophoretic patterns obtained from various protein fractions when the total complement of soluble proteins is separated according to the scheme given. Four soluble proteins are found to be uniquely associated with TMV infection. One of these is the virus itself. As shown in the upper pattern of Fig. 1, the virus protein is readily isolated from the ultracentrifuge pellet obtained from the original extract. As expected, identical treatment of uninfected tissue yields no protein (see right hand uppermost pattern).

When the virus is removed from the original extract and the remaining low molecular weight pro-

teins are brought to pH 3.4, a precipitate is obtained, which on further purification is found to contain only two electrophoretically distinguishable proteins. Identical treatment of uninfected tissue again gives no protein (center patterns Fig. 1). The slower of the components found in the infected preparation has an electrophoretic mobility averaging -3.4×10^{-3} cm²/v/sec at pH 7.0 and is identical with component "B" previously reported by us (2) and with "protein X" of Takahashi and Ishii (3). This protein shall hereafter be designated B3. The second component (designated B6) has an average mobility of about -6.2 at pH 7.0, and is hitherto unreported.

When the low molecular weight proteins soluble at pH 3.4 are purified and examined electrophoretically, the results shown in the lowermost patterns of Fig. 1 are obtained. Infected tissue yields a single component with a mobility of about -4.7 at pH 7.0, whereas no protein is found in the comparable preparation from uninfected leaf. This component, hitherto unreported, has been given the designation A4.

Systemically infected tobacco leaf contains about 50–100 micrograms of B3 and B6, and about one-fourth that amount of A4 per gram wet weight. (The comparable value for TMV is about 2500 micrograms per gram.) The three nonvirus proteins have been found in all preparations made from infected leaf which has been permitted to attain a maximal level of TMV, and they have never been detected in normal leaf. Thus, like the virus itself these components appear in the plant as a specific consequence of infection with TMV.

To provide some insight into the origin of these proteins it is useful to compare their physical, chemical, and biological properties with those of the virus nucleoprotein. Table 1 reveals several significant relationships among these proteins. Unlike TMV, components B3, B6, and A4 are proteins of low molecular weight; their sedimentation constants are similar ($S=3$) and very small as compared with TMV ($S=ca. 100$). Unlike TMV, none of the three proteins contains nucleic acid, as judged by their ultraviolet absorption maxima, and by the usual nucleic acid tests. Unlike the virus, the accessory proteins, when inoculated on TMV-susceptible plants (*N. tabacum* and *N. glutinosa*) are not infectious.

Despite these differences, the nonvirus proteins do show a kinship to TMV. When purified preparations of each of these proteins in phosphate buffer are

¹ Aided by a grant from the National Foundation for Infantile Paralysis.

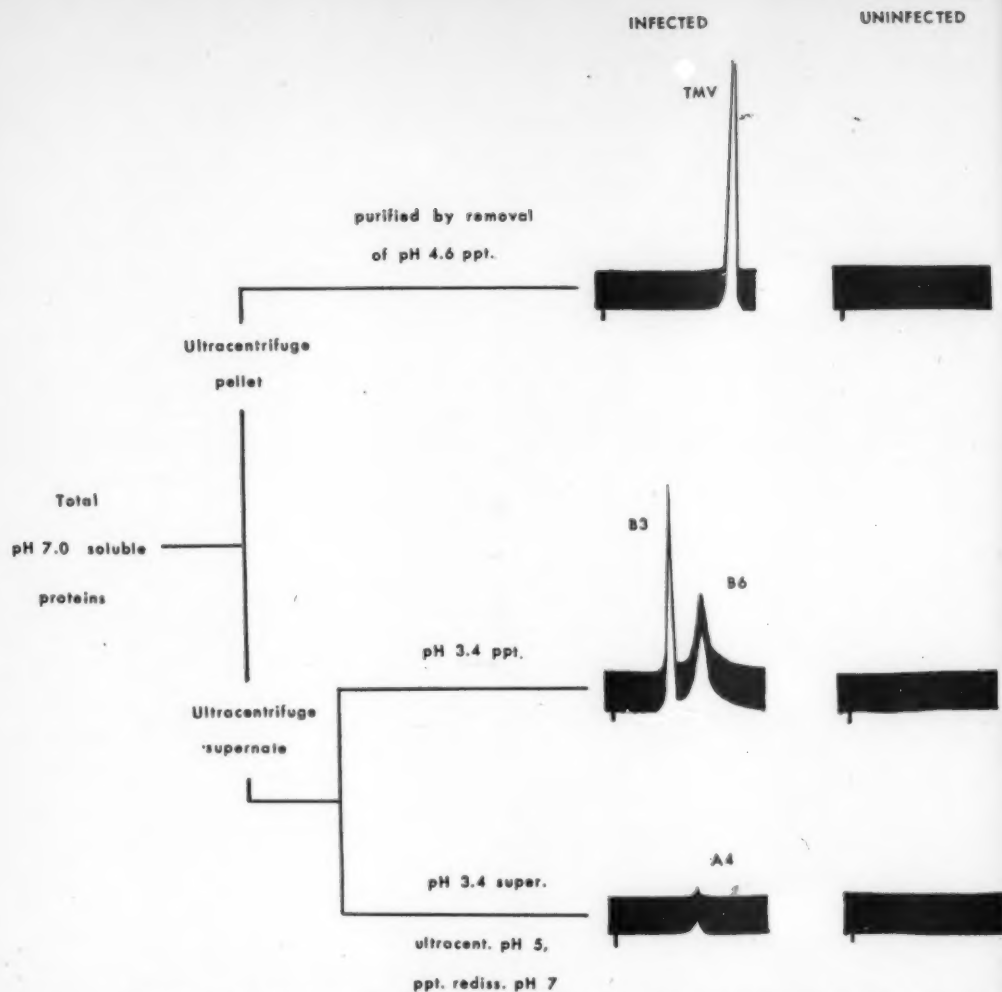


FIG. 1. Ascending electrophoretic patterns obtained from comparable fractions of soluble protein extracts of uninfected (right column) and systemically infected (left column) leaves of *N. tabacum* (variety White Burley). Movement is to the right. All preparations were in 0.05 M phosphate buffer, pH 7.0. Electrophoresis was carried out for 90 min at an average current of 8.5 ma. Ultracentrifugation was carried out for 1 hr at $104,500 \times g$.

brought to pH 5.0, they form high molecular weight aggregates with sedimentation constants in the range 100–200, which readily sediment in the ultracentrifuge. The polymerization of B6 and A4 is reversible, and the original low molecular weight proteins are easily regained when the preparations are returned to pH 7.0. However, the polymerization of protein B3 is irreversible under these conditions. This process appears to involve molecular rearrangement more deep-seated than mere physical aggregation, for the polymerized form has an electrophoretic mobility at pH 7.0 (–8.0) which is considerably different from that of the original B3 (–3.4). The polymerized form of B3 has been designated B8.

There is a suggestive similarity between the geometry of protein B8 and TMV. As can be seen from the electron micrographs (Fig. 2), both are rods of similar size and axial ratio. This observation agrees with the results of Takahashi and Ishii with polymerized "protein X" (4) and is further evidence of the identity of the latter with protein B3. Unfortunately, due to the instability of the polymerized forms of proteins B6 and A4, electron micrographs of these components are not yet at hand.

Thus, while the accessory proteins, as they occur in tissue extracts, are low molecular weight proteins, they are readily converted, *in vitro*, into macromolecules in the size range characteristic of TMV and

TABLE 1
PROPERTIES OF PROTEINS SYNTHESIZED IN THE
LEAVES OF *N. tabacum* AS A RESULT OF
INFECTION WITH TMV

Protein	Average electro- phoretic mo- bility at pH 7.0 cm ² /v/ sec × 10 ⁻³	Ultra- violet absorp- tion maxi- mum, mμ	Sedimen- tation con- stant, pH 7.0	Infect- ivity
TMV	-9.7	280	ca. 100	Infectious
A4	-4.7	280	3	None
B3	-3.4	280	3	None
B6	-6.2	280	3	None
B8*	-8.0	280	ca. 160	None

* B8 does not occur in the leaf as such, but is formed *in vitro* by polymerization of B3.

other plant viruses. These facts, especially the physical resemblance between protein B8 and TMV, might be taken to indicate that such aggregation actually occurs in the infected leaf, and that one or more of the low molecular weight accessory proteins serve as precursors of TMV. However, the aggregation, *in vitro*, of small globular proteins into a macromolecular fibrous product is by no means uncommon among proteins obtained from a variety of sources. For this reason, the conclusion that B3 or another of the accessory proteins is in fact a precursor of TMV must be supported by evidence more specific than that offered by a comparison of electron micrographs.

Data which more firmly establish close relationships among TMV and the nonvirus proteins have been obtained from immunochemical studies. A serum against TMV was prepared by injecting rabbits with an adjuvant emulsion of highly purified electrophoretically homogeneous TMV. The reaction of this serum with TMV, as determined by the quantitative precipitin technique of Heidelberger and Kendall (5) is shown in the upper curve of Fig. 3A. The curve is typical of the reaction of an antigen with its homologous serum, showing an equivalence zone at about 2 mg of antigen. Figure 3A (lower curve) also shows that anti-TMV serum will cross-react with protein B8. The reciprocal relationship is shown in Fig. 3B, which indicates that both B8 and TMV react with a serum prepared against an electrophoretically homogeneous preparation of protein B8.² Similar studies show that proteins B6, B3, and A4 cross-react with anti-TMV serum, and that protein B6 cross-reacts with anti-B8 serum (Fig. 4). Precipitin tests with comparable fractions from uninfected leaf show no reactivity with anti-TMV or anti-B8 serum (Fig. 4). Jeener and Lemoine have recently detected a nonvirus nucleic acid-free antigen which cross-reacts with anti-TMV serum in extracts of infected tobacco plants (6). It is not clear from their data whether the fraction

² These cross reactions have been confirmed by tests conducted in agar diffusion tubes.

studied was B3, B6, or a mixture of both proteins.

It is well established that the occurrence of immunochemical cross reactions between proteins is a clear indication of structural similarity (7). The above results are evidence, therefore, of close structural relationships among TMV and proteins B3 (or its polymer B8), B6, and A4 which do not extend to any normal tobacco protein. Previous observations (1) have shown that the protein fraction from infected leaf that contains B3 and B6 rapidly incorporates N¹⁵ from isotopically labeled host ammonia. Like the virus, these proteins appear to be synthesized *de novo* from ammonia in infected tissue.

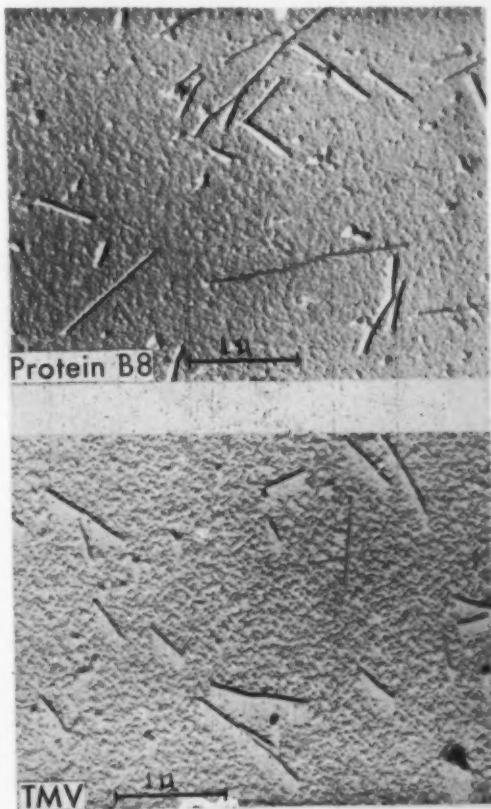


FIG. 2. Chromium-shadowed electron micrographs of TMV and protein B8 obtained from pH 7.0 solutions of these proteins.

It can be concluded therefore that in common with TMV, the nonvirus components that appear in the leaf as a result of infection are specific products of the new paths of protein synthesis brought into action by the entry of the virus inoculum into the host cell. Since the nonvirus proteins appear to be functional components of the process of virus reduplication, any mechanism proposed for the biosynthesis of TMV

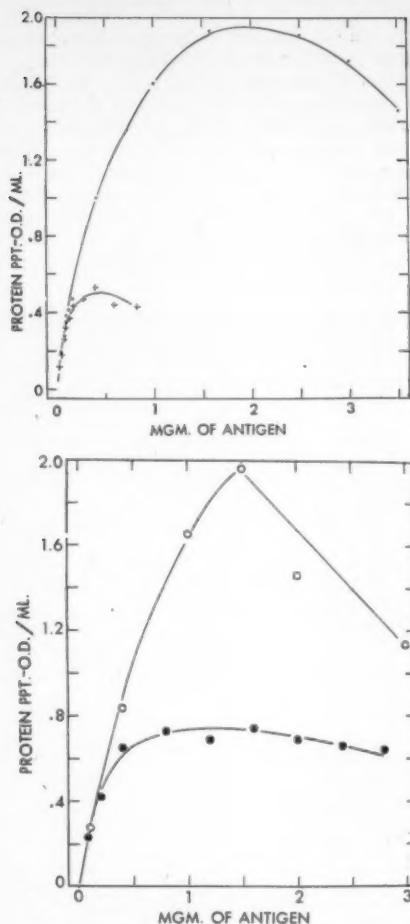


FIG. 3. Precipitin reactions of TMV and protein B8 with rabbit sera prepared against electrophoretically homogeneous TMV and B8. (Above) Precipitate formed by reacting 0.05 ml of anti-TMV serum with indicated amount of TMV (points, upper curve) and B8 (plus signs, lower curve). Optical densities are at 750 m μ and represent color due to Folin phenol reaction of precipitates in 1 ml of reagent. (Below) Precipitate formed by reacting 0.05 ml of anti-B8 serum with indicated amounts of TMV (open circles, upper curve) and B8 (closed circles, lower curve). Ordinate as for 3A.

must also account for the concomitant synthesis of these accessory proteins.

To describe the relationships between the synthesis of TMV and B3, B6, and A4 the amounts of these proteins present in infected tissue after various periods of time following inoculation have been determined with the aid of the immunochemical reactions just described. The results of one such experiment are shown in Figs. 4 and 5. In this experiment, a series of comparable uninfected and infected leaf blade samples were cultured in nutrient under constant conditions for 371 hr following the time of inoculation.

Periodically, infected and uninfected tissue samples were removed, homogenized, and fractionated to yield isolated TMV, A4, B6, and B8 (by polymerization from B3). TMV was determined chemically. The A4 component was estimated by reacting an increasing amount of this fraction with anti-TMV serum and determining the precipitates formed. Similar reactions were carried out between aliquots of the B6 and B8 fractions and anti-B8 serum.

Typical results of such determinations are shown in Fig. 4 for tissue extracted at 371 hr after inoculation.

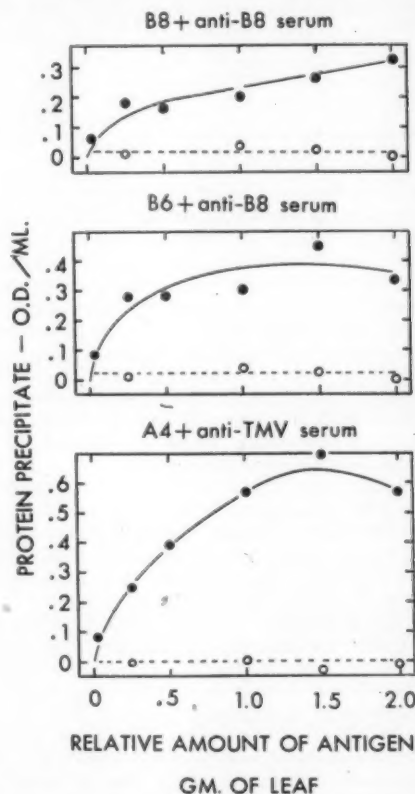


FIG. 4. Precipitin reactions between protein fractions from otherwise identical uninfected (open circles, broken lines) and infected (closed circles, solid lines) tobacco leaf tissue cultured for 371 hr after inoculation with TMV. Ordinate as for Fig. 3. Abscissa indicates the amount of tissue from which the given antigen sample was obtained.

Precipitin reactions were obtained from all three accessory protein fractions derived from infected tissue. On the other hand, no reactions occurred with the same fractions derived from the otherwise identical uninfected tissue. This is confirmatory evidence that the three nonvirus proteins are found in infected leaf but not in normal leaf.

From the initial slopes of curves such as those

shown in Fig. 4 it is possible to estimate the amount of each protein present in a given tissue sample. Measurements of this kind were made for each of the three fractions isolated from uninfected and infected tissue at various times after inoculation. At all times the fractions derived from uninfected tissue gave no precipitin reaction. The results obtained from infected tissue are shown in Fig. 5 together with a curve describing the TMV content of the tissue.

It is apparent that the rates of production of the nonvirus proteins are significantly related to the appearance of TMV itself. None of the nonvirus proteins is detectable until about 220 hr after inoculation, when the TMV content has already attained about one-third its maximum level. Protein A4 rises most rapidly in amount; more than half the final A4 content appears in the 24-hr period just preceding 220 hr. Protein B6 appears somewhat more slowly than A4 at first, but the rate of formation continues at its initial level even after the rate of appearance of both TMV and A4 have leveled off. Protein B3 (determined in the form B8) is not detectable until 280 hr after inoculation, and it is thus the last of the three proteins to occur in the tissue.

The most striking result of these observations is that the nonvirus proteins, A4 in particular, appear quite suddenly at a time which is well beyond the point when TMV is first detected. This suggests that the appearance of the nonvirus proteins has been brought about by some qualitative change in the character of the biochemical mechanisms already engaged in production of TMV; Fig. 5 indicates that this change occurs at about 200 hr after inoculation. The fact that one of the chief differences between TMV and the nonvirus proteins is the latter's lack of nucleic acid suggests that some change in nucleic acid metabolism at 200 hr may act as the stimulus for the abrupt emergence of new products in the infection process at this time.

This suggestion is supported by some preliminary observations on the nucleic acid metabolism of infected and uninfected leaf tissue which were made during the course of the experiment described in Fig. 5. It has been found that a nucleoprotein containing about 20-30 per cent pentose nucleic acid can be extracted from the buffer-insoluble protein of tobacco leaf by a strong salt solution. The amount of this nucleoprotein present in the uninfected and infected tissues just described was determined; the differences in the amounts present in comparable uninfected and infected tissue at various times after inoculation are plotted in the lower curve of Fig. 5. This curve shows that excess nucleoprotein develops in infected tissue before TMV appears (at about 100 hr). Then, as TMV begins to be formed, this excess is reduced until it falls to zero at 203 hr. It is just after this point that the nonvirus nucleic acid-free proteins begin to appear in the tissue.

Determinations of the differences in pentose nucleic acid content of the insoluble nucleoprotein fraction of the tissues discussed above gave results which paral-

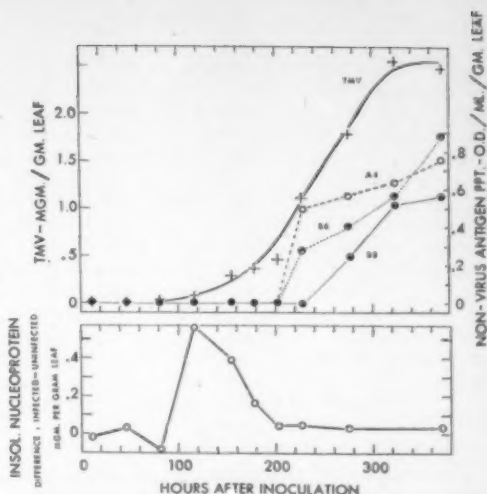


FIG. 5. The amounts of various proteins found in nutrient-cultured tobacco leaf tissue at various times after inoculation with TMV. Virus determined chemically. Proteins A4, B6, and B8 determined immunochemically as described in Fig. 4. The lower curve represents the differences between the nucleoprotein extracted by 10% NaCl solution from insoluble fraction of infected tissue and comparable uninfected samples. Values given are based on micro-Kjeldahl nitrogen determinations.

leled those described in the lower curve of Fig. 5.

In summary, the foregoing results show that in addition to TMV, infected tissue synthesizes *de novo* three noninfectious nucleic acid-free proteins which, on the basis of immunochemical cross reactivity, are closely related to the virus. The nonvirus proteins, like TMV itself, therefore appear to be produced specifically as a result of the new path of protein synthesis induced in the host by inoculation with TMV. However, the accessory proteins are not formed in parallel with TMV, but appear after a rather sudden change (probably associated with depletion of a nucleic acid store) in the character of the biosynthetic process.

It can be concluded that each of the nonvirus proteins plays some specific part in the process of TMV reduplication. For each of the proteins three alternative propositions are consistent with the data:

Alternative 1. Nonvirus protein and TMV are sequential products of the same protein-synthesizing mechanism, i.e., nonvirus protein may act as an actual precursor of TMV. This proposition would mean that the nonvirus protein is produced at all times by the TMV-synthesizing mechanism and is converted to TMV at a variable rate. The early absence of the nonvirus protein might be accounted for by rapid and complete conversion to TMV. The sudden appearance at 200 hr might result from depletion of the previously synthesized nucleic acid required to convert it to TMV. The possible assignment of precursor roles to one or more of the nonvirus proteins introduces an interest-

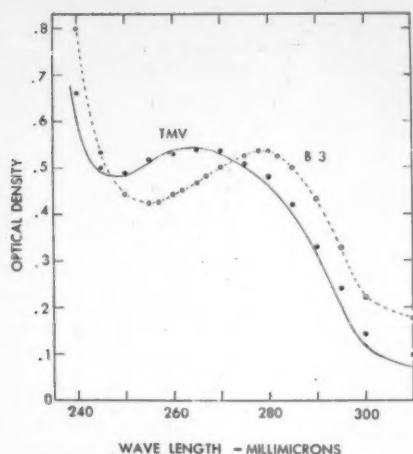


FIG. 6. The ultraviolet absorption spectra of protein B3 (open circles, dotted line), TMV (solid line), and a complex of protein B3 with nucleic acid prepared from TMV (closed circles).

ing experimental approach to the problem of TMV synthesis: an attempt to induce infectivity in the nucleic acid free presumed precursor by the addition, *in vitro*, of nucleic acid obtained from TMV. Proteins frequently form nonspecific *in vitro* complexes with nucleic acid. The absorption spectrum of such a complex between B3 and TMV nucleic acid is illustrated in Fig. 6. This product was not infectious. It is, of course, presumptuous to suppose that the mere mixing of the two components in simple solution would accomplish what must be in the living cell a highly specific, structurally oriented process. Nevertheless, such studies may shed light on the intracellular behavior of the nonvirus proteins.

Alternative 2. Nonvirus protein is an alternative

rather than sequential product of the mechanism that produces TMV and appears during the course of virus synthesis as a result of a sudden loss in specificity of the synthesizing processes.

If this were the case, a rather close resemblance of the new products (i.e., A4, B6, B3) to the old one (TMV), such as that revealed by immunochemical cross reaction, is to be anticipated. Such an event might be usefully thought of as a mutation, and the nonvirus protein as a noninfectious "mutant" of TMV, or perhaps a low molecular weight breakdown product of such a "mutant."

Alternative 3. Nonvirus protein is part rather than product of the TMV-synthesizing apparatus of the cell. If this were the case, our observations would show that: (a) the parts of the apparatus represented by nonvirus protein are synthesized *de novo* subsequent to inoculation and do not antedate the entry of the inoculum; (b) these parts of the virus-synthesizing mechanism bear a close structural similarity to TMV; (c) the soluble nonvirus protein detected in tissue extracts is probably sloughed off from an insoluble cell component; and (d) this degeneration of the TMV-synthesizing apparatus begins at about 200 hr after inoculation, and is possibly associated with depletion of a source of pentose nucleic acid.

Experiments bearing on these alternative propositions are in progress.

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Birmingham Conference on Nuclear Physics

Ernst Bleuler

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AN international conference on nuclear physics, arranged by the departments of physics, electron physics, and mathematical physics, was held at the University of Birmingham, July 13th to 18th, 1953. It was attended by about two hundred fifty visitors, thirty of them from America. The chief topic of the conference was the complex nucleus; cosmic rays and meson physics proper were not discussed, nucleon-nucleon collisions only briefly. This wise concentration allowed a reasonably detailed treatment of the different items on the program. Each session was opened by a summarizing

talk on the present status of the subject which was followed by short contributions and ample discussion.

Rather than reviewing the whole conference chronologically, some of the results of the discussions will be presented. References will be given sparingly, and will pertain only to the speaker.

Nuclear Radii. The $2p_{1/2}$ transition of μ -mesons, the diffraction pattern for high-energy particles, and the isotope shift seem to indicate nuclear radii somewhat smaller than the usual value of 1.45 to 1.50×10^{-13} A $^{1/3}$ cm. An irregular variation is found between Be 9 and O 16 , both from neutron cross sections and the

stripping interaction distance, Be^9 being high, C^{12} low (Bonner, Holt).

The diffraction pattern of 125- to 150-Mev electrons from heavy nuclei does not show the maxima and minima expected for a uniform charge distribution, but agrees with an exponentially decreasing density whose rms radius has about the normal value (Hofstadter). This result, however, is expected to be modified by further theoretical treatment.

Nuclear Spectroscopy. Advances in the different techniques were discussed. A more refined deuteron stripping theory takes into account the reaction of the outgoing proton (Messiah). It yields smaller cross sections than the original Butler theory; larger reduced widths are thus deduced from the experiment. The n - p interaction in the deuteron is still neglected. In view of a rapid variation of the angular distribution pattern with deuteron energy observed by Parkinson, the question of interference between the stripping process and compound nucleus formation with possible resonance features was discussed, without conclusion. The analysis of the patterns into contributions from different angular momenta seems rather unreliable.

The interpretation of angular correlations of successive radiations is subject to the uncertainties due to the influence of extranuclear fields. In the classical case of In^{111} (Cd^{111}) the electric quadrupole interaction was shown to be responsible for the diminished anisotropy observed with most solid sources. From measurements with a variable magnetic field parallel to the electric field gradient in a single crystal, both the magnetic and the electric coupling constants can be deduced. Most liquid sources show the full anisotropy and are thus suitable for analysis. This seems to be due to the rapid change of the external fields. In liquids with long relaxation times, e.g., glycerin at normal temperatures, the anisotropy is decreased (Heer, Novey).

The powerful tool of conversion measurements has been further improved by more accurate determination of the dependence of α_K/α_L on gamma-ray energy and atomic number. The analysis of the angular distribution of the two partners of internal pair conversion has been applied successfully (Devons).

Radiative widths can be determined by coincidence methods down to decay times of a few 10^{-10} second. In addition to the old methods of comparison with particle widths and neutron resonance widths (Kinsey), two new procedures were applied for levels that decay to the ground state. In resonance scattering the energy gap due to the recoil of the emitting and the absorbing nucleus is bridged either by mechanical motion (Moon, Davey) or by temperature motion (Malmfors). The scattering intensity is then proportional to the level width and measurable for decay times less than a few 10^{-11} second. On the other hand, the level width can be determined by measuring the cross section for the excitation by the Coulomb field of bombarding particles (Huus). Still, a general method for the measurement of decay times between 10^{-9} and 10^{-12} second is lacking.

Nuclear Models. The basis of most of the discussions was the shell model, in the Mayer-Jensen variation. For the levels of the light nuclei the isotopic spin is nearly a good quantum number, the intensity of admixtures being of the order of 10^{-3} to 10^{-2} , as expected from the Coulomb interaction alone (Wilkinson). For the ground state and first excited state of N^{13} and C^{13} , the reduced and radiative widths and the magnetic moments can be explained by intermediate coupling (between ls and jj) with the same parameter that also gives the best overall agreement with the empirical level schemes (Lane). Low-lying many-particle levels in the $f_{7/2}$ shell were reported for N or $\text{Z}=23, 25$, i.e., for 3 particles or holes; they are absent, as expected, for N or $\text{Z}=21, 27$ (Nussbaum). A beautiful scheme of ten levels in Pb^{208} was reported, which is in very good agreement with the expectation for two neutron holes and jj coupling (Alburger, Pryce).

The treatment of heavy nuclei with partly filled large subshells is controversial. In the individual-particle approach (Flowers), all properties are calculated with the aid of the unfilled shell only. It gives, therefore, the characteristic strong variations near the ends of each shell; the mathematical difficulties in the middle of the large shells, however, are considerable. They are avoided in the collective model (A. Bohr) which treats the whole nucleus (again) as a "liquid drop" whose surface oscillations are coupled to the motion of the individual particles. The lowest excited states, thought to be surface waves of an irrotational liquid, can be described like rotational levels. Experimental support for this picture is claimed to be furnished by regularities in the level energies and the spin assignments obtained from alpha fine structure and conversion data, by the agreement of the electric quadrupole moments of the excited states (which are deduced from the Coulomb-field excitation) with that of the ground state and, quite generally, by the large quadrupole moments and $E2$ transition probabilities. The model, in its simplest form, does not give good agreement with the experiments near the shell ends. The discussion between the exponents of the two models continued throughout the conference week, with an apparent gradual rapprochement of the viewpoints.

Nuclear Reactions. The discussion dealt chiefly with the validity of the N. Bohr assumption about the formation of a compound nucleus. The total averaged neutron cross sections from 0 to 3.5 Mev and the angular distributions of elastically scattered 1-Mev neutrons may be explained by a single-particle theory using a potential well of conventional radius and depth $-V = V_0(1 + \xi^2)$, with $V_0 = 19$ Mev, $\xi = 0.05$ (Barshall). Despite the small value of the imaginary part of the potential which corresponds to a mean free path of the order of 10^{-13} cm, compound nucleus formation is not unimportant because of the many internal reflections of the neutron wave. This is evidenced by the cross sections for inelastic neutron scattering at 3, 4.5, and 14.5 Mev which show nearly "black" nuclei (Bonner), and by the isotropic distribution of inelastically scattered neutrons ($E < 4$ Mev)

for a primary energy of 14 Mev (Rosen) and inelastically scattered protons ($E < 10$ Mev) for a primary energy of 18 Mev (Gugelot). Unfortunately, the above potential cannot be used to explain the angular distribution of elastically scattered protons. For Al, at 18 Mev, one would need $V_0 = 45$ Mev, $\xi \approx 0.5$; for Cu and heavier elements, no choice of parameters is satisfactory.

Attempts to determine level densities from the energy distribution of reaction products uncovered some queer facts. The high-energy part of the spectrum of inelastically scattered protons is more intense than expected from any expression for the level density. Furthermore, the shape of the spectrum is essentially independent of the primary energy while it is supposed to reflect the level density of the residual nucleus whose excitation energy varies with the primary energy. It is not clear, at the moment, if these deviations from the compound nucleus, evaporation picture can entirely be attributed to other processes, such as surface reactions or electric energy transfer (Gugelot).

Measurements on some reactions involving the lightest nuclei were reported. There still does not seem to be clear evidence for an excited state of He^4 ; the He^5 doublet could not be observed in the He^3 (T, p) He^5 reaction (Good).

Polarized Beams and Nuclei. The polarization of beams is a direct consequence of spin-dependent forces. The polarization of d, d -neutrons was detected by scattering on carbon and found to be about 20 per cent at 700 kev deuteron energy (Huber, Ricamo). The polarization of 240-Mev protons, produced by scattering on different elements, and detected by a second scattering process, is about 20 per cent for H, Al, Si, 30 per cent for Ag, and 50 per cent for Li, Be, B, C, Cu (Kaplon).

As an example of the information to be gained from the measurement of the anisotropy of the gamma radiation emitted by aligned nuclei, the case of Co^{58} was discussed (Grace). The distribution gives a spin $I = 2$ for the excited state of Fe^{58} , is compatible with Gamow-Teller selection rules only, and the temperature dependence indicates a magnetic moment of about 3.5 nuclear magnetons for Co^{58} .

Instruments and Accelerators. The discussion of instruments was limited to cloud chambers and scintilla-

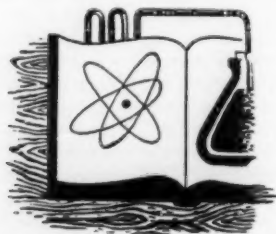
tion techniques. The bubble cloud chamber, diffusion chambers, and a conventional chamber with an internal trigger system, essentially a proportional counter, were presented. With the latter it was possible to show that the previously reported ternary fission events, with all three particles heavier than alphas, are spurious, the third heavy track being due to a knock-on nucleus (Berthelot).

Applications of the scintillation technique that were discussed included a total absorption spectrometer for electrons or gamma rays of more than 50 Mev (Hofstadter) and an efficient counting system for slow and medium fast neutrons employing the counting of the gamma rays emitted after neutron capture in B^{10} (Gray).

Topics treated in the session on accelerators were the acceleration of sixfold charged N and O ions in the Birmingham 60-inch cyclotron, with beams of the order of 10^{-9} ampere (Walker); a method for obtaining the shape of a cyclotron beam pulse without recourse to widest-band amplifiers; and the design of several high-voltage machines, including the cosmotron injector.

Nuclear Forces. The discussion of the meson theory of nuclear forces was essentially a review of the present situation. It dealt with the $T = 3/2, I = 3/2$ resonance in $\pi - p$ scattering and photoproduction of π mesons, the Lévy theory—which gives potentials in agreement with the experiment, but contains errors and does not seem to converge—the effective range potentials for the low-energy np and pp data, and the phase analysis for the high-energy data. For the latter, it was shown experimentally that the distribution of np scattering at 135 Mev is not symmetrical with respect to 90° , but shows a predominant backscattering (Snowden). No great theoretical progress seems to have been made for some time.

It was a happy coincidence that during the meeting the Birmingham proton synchrotron attained its maximum energy, around 1000 Mev. All visitors felt that there could scarcely have been a better compensation for the magnificent work done by Professors Burcham, Moon, and Peierls, the conference secretaries Professors Field and Riddiford, and the entire staff of the physics departments in preparing this conference.



The Effect of Exposure to the Atomic Bombs on Pregnancy Termination in Hiroshima and Nagasaki: Preliminary Report¹

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FOR THE PAST SEVEN YEARS a comprehensive program of investigation of the potential delayed effects of exposure to the atomic bombs has been in progress in Hiroshima and Nagasaki, Japan. One facet of this program has been an attempt to provide answers to the following two questions:

1. Can there be observed, during the first year of life, any differences between children conceived subsequent to the atomic bombings of Hiroshima and Nagasaki, one or both of whose parents were exposed to the effects of the bombings, and the children born to suitable control parents?

2. If differences do exist, how are these to be interpreted?

The present communication is based on a preliminary analysis of a portion of these studies. A more complete account will appear at a later date.

The data of this study have been collected as follows. During and ever since World War II there has been in effect in Japan a system of rationing of food and other items. Under this system, any woman reaching the fifth month of pregnancy is, upon certification of the fact by an obstetrician or midwife, granted certain special ration privileges. Because of the economic stringencies of postwar Japan, pregnancy registration approached the 95 per cent level during the period covered by this study. A plan was developed whereby

at the time of registration for ration purposes, each pregnant woman or her representative in Hiroshima and Nagasaki completed in duplicate the first two-thirds of a questionnaire which dealt with identifying information, location and symptoms at the time of the atomic bombing, past reproductive performance, and certain details concerning the present pregnancy. The final third of the form, of necessity left blank at the time of registration, included such items as type of termination (stillbirth or livebirth, premature or term), sex, birth weight, and occurrence of malformation. One copy of this form was then given the registrant, the other copy retained by the Commission. At the termination of her pregnancy, each registrant gave her midwife or obstetrician the registration form for completion. In the event of a termination in some way abnormal, the attendant was requested to contact the Commission at once. In the event of an apparently normal termination, on the other hand, the attendant retained the form until collected by a Commission representative, on an approximately weekly schedule. In either event, the newborn child was examined by a physician in the employ of the Commission—as soon as possible if the termination was abnormal, on a more leisurely schedule if reported normal. Autopsies have been performed on as many children who were stillborn or died during the neonatal period as possible. Approximately one-third of the children examined at birth have been reexamined at age nine months.

The duplicate registration forms were used to establish a file based on expected date of confinement. Follow-up studies were instituted if there was no report of the termination of a pregnancy a month after the expected date of confinement. In this way, data were obtained on the outcome of the great majority of registered pregnancies. The chief loss of information involved women who moved out of the two cities subsequent to registration.

For a variety of reasons, in this study the most reliable indices of the amount of irradiation received by a survivor of the bombings were felt to be distance from the hypocenter (the point directly beneath the bomb when it exploded) and the subsequent development of the following symptoms or combination of symptoms: epilation, petechiae, and/or gingivitis. On

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The material herein summarized represents the work of many hands in addition to those of the authors. It is particularly appropriate to express our deep gratitude to the Japanese parents, physicians, and midwives, without whose cooperation this study would not have been possible. Finally, it is a pleasure to acknowledge the support of the members of the Committee on Atomic Casualties of the National Academy of Sciences—National Research Council, and the Division of Biology and Medicine of the U.S. Atomic Energy Commission.

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the basis of position at the time of the explosions and the development of symptoms, each parent has been placed in one of the following five radiation categories:

Group 1. Not in Hiroshima or Nagasaki at the time of the bombings. These individuals are either residents of the city who for a variety of reasons were not there at the time of the bombings, or persons who have moved into the city subsequent to the bombings (August of 1945). Approximately two-thirds of the husbands and wives registered in connection with this program fall into this category.

Group 2. In one of the two cities at the time of the bombings, but at distances in excess of 2544 meters from the hypocenter, and not developing any of the cardinal radiation symptoms enumerated above.

Group 3. In one of the two cities and within 1845 to 2544 meters of the hypocenter, but asymptomatic with respect to the cardinal symptoms.

Group 4. In one of the two cities, and less than 1845 meters from the hypocenter, but asymptomatic. Most of these individuals were shielded to a greater or lesser extent from the full effects of the bombs.

Group 5. In one of the two cities, and developing one or more of the cardinal symptoms during the several months following the bombings.

The estimation of the average amount of whole body irradiation, both gamma and neutron, received by the individuals falling into groups 2 to 5 presents a number of problems. Individuals in group 2 probably received on the average only the equivalent of a few roentgen units. On the other hand, group 5 individuals probably received the equivalent of between 200 and 600 r, with the average in the neighborhood of 300 r. Group 3 and group 4 individuals received intermediate dosages, difficult to estimate because of the shielding factor, with group 4 definitely receiving more on the average than group 3.

The possible observable genetic effects of irradiation upon the first generation born after an atomic bombing are many and varied. The indicators utilized in this study were: type of termination (livebirth or stillbirth), sex of child, birth weight, and occurrence of gross congenital malformation. *Each of these possible indicators of genetic damage is also influenced by a number of other factors; there are no unique yardsticks of a genetic effect.* Under these circumstances, the crux of any program of study was the feasibility of establishing a control population which, in so far as possible, differed from the irradiated only with respect to the radiation factor.

Between 1948 and 1952 the outcome of 31,034 pregnancies was determined in Hiroshima, and 31,073 in Nagasaki. A detailed comparison, by city, of the fathers and mothers falling into the five radiation groups has been carried out with respect to age, parity, consanguinity, economic status, incidence of positive serological tests for syphilis, and parental co-operation. Significant differences were found to exist with respect to the first three points of comparison. Although the known relationships of age, parity, and consanguinity to the sex ratio are slight, there exists

a considerable literature, substantiated in part in our own data, to indicate significant relationships between age, parity, and consanguineous marriage, on the one hand, and the frequency of stillbirths, birth weight, and the frequency of gross malformations on the other. It is apparent that provision for these differences must be made in the analysis of the data. The further point should be mentioned that, in contrast to the parents falling into radiation categories 2, 3, 4, and 5, more of the individuals in radiation group 1 had previously resided in rural areas or outside the Japanese islands (e.g., Korea, Manchuria).

In addition to the differences between the parents found in radiation groups 1 to 5 described in the preceding paragraph, there exists at least one other important difference between the individuals falling into the various radiation categories. Late somatic effects of irradiation have been established as occurring in a small fraction of relatively heavily irradiated persons. These include cataracts (1) and leukemia (2). Other more subtle effects may exist. In view of the known relationship between maternal health and certain of the indicators of possible genetic damage, *extreme caution must be exercised in the genetic interpretation of any apparent effect of irradiation mediated solely by the mother.*

The various possible indicators of genetic damage are not independent of one another. Thus, gross malformation and stillbirth are correlated. It was apparent that some allowance had to be made for this fact before the various indicators could be regarded as independent guides to a radiation effect.

With the foregoing considerations in mind, a plan of analysis has been evolved, the first step of which is to subdivide the data as follows:

A—mothers less than 35 years of age and unrelated to their spouses. This amounts to approximately 84 per cent of the Hiroshima and 77 per cent of the Nagasaki registrations.

B—mothers 35 years of age or older and unrelated to their spouses, approximately 10 per cent of the Hiroshima and 15 per cent of the Nagasaki material.

C—mothers related to their spouses, approximately 6 per cent of the Hiroshima and 8 per cent of the Nagasaki material.

Except with reference to the sex ratio, only the *A* data will be considered in the results to be presented. Exclusion of the *C* data from consideration at this time removes the known consanguinity differences, while exclusion of the *B* data very materially reduces the age differential, although significant differences remain. For example, in the Hiroshima data, exclusion of the *B* data reduces the average age difference between radiation group 1,2 and group 4,5 mothers from 3.5 to 1.9 years, whereas in Nagasaki the corresponding reduction is from 1.9 to 0.5 years. Furthermore, inasmuch as significant differences exist between Hiroshima and Nagasaki with respect to age, parity, consanguinity, and anthropological background, and since the proportions falling in the five radiation groups differ for the two cities, the results for the

TABLE 1
COMPARISON OF CERTAIN CHARACTERISTICS OF CHILDREN OF PARENTS FALLING
INTO DIFFERENT RADIATION GROUPS

The numbers 1, 2, 4, and 5 as applied to the parents designate the radiation exposure group as defined in the text. Arrows directed upward indicate agreement with genetic hypothesis; the downward-pointing arrows, disagreement. Numbers in parentheses in the columns under the headings Hiroshima and Nagasaki indicate the number of observations.

Indicator	Comparison	Hiroshima	Nagasaki	Significance of difference (normal deviate)		
				Hiroshima	Nagasaki	
a. Both parents radiation group (1, 2) vs. both parents (unless otherwise indicated) radiation group (4, 5)						
Proportion of male births (All data)	Both parents (1, 2)	vs. Mother (4, 5) Father (1, 2)	0.5194 (21737)	0.5102 (3003) 0.5190 (26256)	0.4837 (1445)	0.948 ↑ 2.615 ↑
	Both parents (1, 2)	vs. Mother (1, 2) Father (4, 5)	0.5194 (21737)	0.5166 (962) 0.5190 (26256)	0.5376 (785)	0.170 ↓ 1.030 ↑
Proportion of mal-formed infants (A data)	Both parents (1, 2)	vs. Both parents (4, 5)				
		Male infants	0.0115 (9537)	0.0045 (222) 0.0096 (10409)	0.0145 (69)	1.515 ↓ 0.340 ↑
		Female infants	0.0107 (8801)	0.0127 (236) 0.0101 (9694)	— (69)	0.271 ↑ —
Proportion of stillbirths (A data)	Both parents (1, 2)	vs. Both parents (4, 5)				
		Male infants	0.0209 (9427)	0.0498 (221) 0.0182 (10309)	0.0147 (68)	1.965 ↑ 0.239 ↓
		Female infants	0.0202 (8707)	0.0258 (233) 0.0148 (9596)	0.0145 (69)	0.534 ↑ 0.021 ↓
b. Both parents radiation group (1, 2) vs. at least one parent radiation group (5)						
Proportion of male births (All data)	Both parents (1, 2)	vs. Mother (5) Father (1, 2)	0.5194 (21737)	0.5258 (814) 0.5190 (26256)	0.4801 (477)	0.359 ↓ 1.685 ↑
	Both parents (1, 2)	vs. Mother (1, 2) Father (5)	0.5194 (21737)	0.5187 (347) 0.5190 (26256)	0.5061 (189)	0.026 ↓ 1.302 ↑
Proportion of mal-formed infants (A data)	Both parents (1, 2)	vs. At least one parent (5)				
		Male infants	0.0115 (9537)	0.0081 (618) 0.0096 (10409)	0.0132 (803)	0.903 ↓ 0.543 ↑
		Female infants	0.0107 (8801)	0.0139 (577) 0.0101 (9694)	0.0134 (298)	0.641 ↑ 0.489 ↑
Proportion of stillbirths (A data)	Both parents (1, 2)	vs. At least one parent (5)				
		Male infants	0.0209 (9427)	0.0294 (618) 0.0182 (10309)	0.0134 (299)	1.218 ↑ 0.700 ↓
		Female infants	0.0202 (8707)	0.0246 (569) 0.0148 (9596)	0.0272 (294)	0.660 ↑ 1.296 ↑

two cities will be presented and analyzed separately.

In order to render the indicators independent of one another, the first attribute considered in the analysis was the sex ratio, and the second, frequency of malformation. All grossly malformed infants were then excluded from further consideration, and the frequencies of stillbirths in the various radiation groups obtained. Stillborn infants were then excluded from further consideration, and birth weights were examined. Thus the frequencies of stillbirths within the various exposure categories are based only on those infants with no clinically apparent major malformation. Similarly, mean birth weights are based only on

those liveborn infants without clinically recognizable gross malformations.

The significance of the observed differences between the children of parents with different radiation histories has been tested by the method of fitting constants to a basically 5 × 5 table in which the columns correspond to paternal radiation exposure group and the rows to the maternal radiation exposure group. In addition, selected comparisons have been made. In this paper, because of space limitations, when dealing with the attribute data (sex ratio, malformation frequency, stillbirth frequency), only the results of two comparisons will be presented. These are (1) a com-

parison between the children of parents, both falling in radiation group 1 or 2, and the children of parents, both falling in group 4 or 5, and (2) a comparison of the findings in the children of parents, both falling in radiation group 1 or 2, and the children of parents, at least one of whom falls in radiation group 5. In the first comparison, the amount of radiation which the group 4,5 parents jointly received varies from approximately 300 to 1000 r units of radiation, while in the second comparison, where at least one parent is in group 5, the joint radiation exposure varies from about 200 to 1000 r units. This presentation involves only a portion of the data; this action is considered justified in a preliminary report because this is the most critical comparison in terms of radiation dosage. With respect to the single metrical characteristic (birth weight), the findings are presented as the results of an analysis of variance of the 5×5 table mentioned above. In passing, it should be emphasized that the results of other analyses do not differ materially from the comparisons given in Tables 1 and 2. We will consider now the four sets of results shown in the tables.

1. *Sex ratio* (Table 1). Conventional genetic theory suggests that irradiation of the mother should decrease the percentage of males among her offspring, because the males will be affected by induced sex-linked recessive lethals which will not affect females. Radiation of the father, on the other hand, should result in a decrease in the percentage of females among his offspring, due to the action of sex-linked dominant mutations. Any attempt to postulate the magnitude of the differences at a particular radiation level is rendered difficult by many factors, including the present unsatisfactory state of knowledge concerning the homologous segments of the X and Y chromosomes. It is apparent that in Nagasaki the observed differences are as suggested by hypothesis and, when the factor of direction is considered, significant. The differences remain significant when the comparison is limited to the group 2,3 and the group 4,5 parents. However, this finding does not appear in the more numerous Hiroshima data.

2. *Frequency of malformation* (Table 1). It is a reasonable assumption that induced dominant mutations should result in an increase in the frequency of gross malformations among the children of survivors. Several years ago, as reported by Bugher (3), there appeared to be some evidence that gross malformations were slightly more frequent among the children of exposed parents than among the children of control parents. The present more extensive data fail to confirm this impression.

3. *Frequency of stillbirths* (Table 1). Induced dominant mutations might also be expected to increase the number of stillbirths. The overall trend is in the direction of hypothesis, but the findings approach the level of significance in only one of the four comparisons of Table 1a, that concerned with male infants born in Hiroshima, and none of the comparisons of Table 1b. A supplementary analysis of all the Hiroshima data

TABLE 2
ANALYSIS OF BIRTH WEIGHT DATA BY METHOD
OF FITTING CONSTANTS

In the two tables on which this analysis is based, the rows are composed of the five maternal exposure groups and the columns of the five paternal exposure groups. The sexes have been analyzed separately.

Source of variation	S.S.	D/F	M.S.	F
<i>a. Hiroshima—analysis of variance</i>				
Test for sex				
Fitting m, b_j, c_k^*	259	8		
Difference	3112	1	3112.00	155.99†
Fitting m, a_i, b_j, c_k	3371	9		
Test for mother's exposure				
Fitting m, a_i, c_k	3246	5		
Difference	125	4	31.25	1.57
Fitting m, a_i, b_j, c_k	3371	9		
Test for father's exposure				
Fitting m, a_i, b_j	3220	5		
Difference	151	4	37.75	1.89
Fitting m, a_i, b_j, c_k	3371	9		
Test for interaction				
Fitting m, a_i, b_j, c_k	3371	9		
Difference	1204	40	30.10	1.51‡
Between classes	4575	49		
Between classes	4575	49	93.37	4.68†
Within classes	484126	24260	19.95	
Total	488701	24318		
<i>b. Nagasaki—analysis of variance</i>				
Test for sex				
Fitting m, b_j, c_k^*	503	8		
Difference	3413	1	3413.00	167.63†
Fitting m, a_i, b_j, c_k	3916	9		
Test for mother's exposure				
Fitting m, a_i, c_k	3670	5		
Difference	246	4	61.50	3.02‡
Fitting m, a_i, b_j, c_k	3916	9		
Test for father's exposure				
Fitting m, a_i, b_j	3634	5		
Difference	282	4	70.50	3.46†
Fitting m, a_i, b_j, c_k	3916	9		
Test for interaction				
Fitting m, a_i, b_j, c_k	3916	9		
Difference	1161	40	29.03	1.43‡
Between classes	5077	49		
Between classes	5077	49	103.61	5.09†
Within classes	460899	22641	20.36	
Total	465976	22690		

* m = mean.

a_i = constants fitted for sex.

b_j = constants fitted for five categories of maternal exposure.

c_k = constants fitted for five categories of paternal exposure.

† Significant at one per cent level.

‡ Significant at five per cent level.

arranged in a 5×5 table according to the radiation

groups of the father and mother indicates that the effect is a function of mother's exposure, with a significance at the 0.02-0.05 level. The above mentioned stricture regarding maternal somatic effects is especially pertinent in this respect.

4. *Birth weight* (Table 2). Induced mutations might be expected to impair the metabolic processes of the fetus, and so decrease birth weight, i.e., the children of the more heavily irradiated parents might be expected to weigh less at birth. In both cities the interaction terms are significant at the 0.01-0.05 level. Constants are being refitted to these data taking cognizance of this fact. If these interactions are accepted as real, the tests of main effects are only approximate. The latter reveal no differences in Hiroshima but in Nagasaki the effect of both maternal and paternal exposure is at the level of significance. The differences are, however, in a direction contrary to hypothesis. The explanation of this finding is not readily apparent. It is not borne out by a comparison utilizing only radiation categories 2, 3, 4, and 5, nor are there height-weight differences in relation to parental radiation history among the children re-examined at age 9 months. As noted earlier, there are differences in mean parity between the mothers falling into the various radiation exposure groups, such that where both the mother and father had been relatively heavily irradiated there is a tendency for the mother to have borne more children at the time of this study. Inasmuch as parity is significantly related to birth weight (4), and since the parity differences have not been entirely eliminated by the truncation of the data which has been described, this may account for at least a portion of the findings with respect to birth weight.

The interpretation of the combined results of independent tests of significance, such as are presented in Tables 1 and 2, poses a number of problems, the solutions of which are not entirely clear at present. Furthermore, although truncation of the data at a maternal age of 35 has reduced the age and parity differential between the various radiation groups, there still remain significant differences. Since certain additional data are yet to become available and certain analytic possibilities remain to be explored, it would

appear that an attempt at this time at a definitive interpretation would be premature.

Even in this preliminary note, however, it should be pointed out that these findings, if taken at face value, are entirely consistent with what is known of the radiation genetics of a wide variety of plant and animal material, including *Drosophila* and mice. It is important to emphasize that the conditions of these observations, as well as the fact that they are confined to the first post-bomb generation, permit the detection of only a small fraction of the total genetic effect of exposure to an atomic bomb. Given our estimates of the radiation dosages involved, it has, by analogy with what is now known of radiation genetics, always been doubtful whether significant findings attributable to the genetic effects of irradiation would be apparent in the first post-bomb generation. It is of interest that of the four indicators herein discussed, the one with respect to which the evidence of a significant effect is strongest—sex ratio—is the one that most biologists would probably feel has the largest genetic component in its etiology. This apparent effect on sex ratio may be related to the relatively high proportion of all known inherited traits which is sex-linked in man in contrast, e.g., to the mouse, cat, or dog. An attempt to extend the sex ratio findings is in progress. There is no indication from this study of any "unusual" sensitivity of human genes to irradiation.

It is apparent from the table that the actual amount of critical material is small. It must be emphasized that this is the total material available during the period covered by this study in the cities of Hiroshima and Nagasaki. The only way that sample size could be increased would be through an attempt to trace the relatively few "heavily" irradiated survivors who have established residence elsewhere, an undertaking that has not appeared feasible nor sufficiently profitable in view of the additional effort and expense such an undertaking would require.

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News and Notes

National Meeting of American Chemical Society

THE chemical synthesis of sucrose was among the major advances reported at the American Chemical Society's 124th national meeting, held in Chicago September 6 through 11. A total registration of exactly 10,000 made it the largest ACS meeting ever held outside New York, and the Society set another record when its membership reached 70,000 during the week.

A 33-year-old Canadian chemist, Raymond U. Lemieux, announced the sugar synthesis, which solved a problem that had baffled Emil Fischer and virtually every other carbohydrate chemist for the past half century. Working with George Huber, a 25-year-old Swiss postdoctoral research fellow, in the Prairie Regional Laboratory of the Canadian National Research Council at Saskatoon, Lemieux tackled the project last April despite overwhelming evidence that it could not be done. By June they succeeded in making sucrose

out of derivatives of glucose and fructose, which had been made synthetically by previous investigators. Lemieux and Huber also synthesized maltose and a less common sugar, trehalose, in the course of their experiments.

Since natural sucrose is both abundant and cheap, the synthetic product is unlikely to find commercial application, but the Lemieux-Huber feat represents a significant contribution to carbohydrate chemistry which promises to make the synthesis of many complicated substances a matter of easy routine.

America's chemists and chemical engineers were challenged by ACS President Farrington Daniels of the University of Wisconsin to turn their attention to the food and fuel needs of future generations and to embark at once upon a long-range research program designed to meet those needs. In his presidential address at a general session of the meeting, he warned his audience that present resources of many types are dwindling and that imaginative and far-reaching investigations must be started to "insure that our children's children may have a continuation of the fuel, food, metals, and materials which we are so freely enjoying and so rapidly consuming."

An authority on both atomic and solar energy, Farrington Daniels emphasized the necessity of learning how to use them economically as sources of industrial power before existing gas, oil, and coal reserves are too far depleted. Dr. Daniels made it clear that he was not talking about any imminent shortage of these fuels, but said that "according to optimistic guesses, in a few hundred years, or at best a couple of thousand, the world's supply will be nearly gone."

Coupled with Dr. Daniels' appeal for early attention to the needs of the future was a call for a bolder approach to the whole field of research and development. He advocated more "risk research" which, like risk capital investments, may be lost but which on the other hand may bring in large returns, and he also urged a less timid attitude toward getting promising laboratory achievements into the pilot plant stage—even though this may prove costly if a project does not succeed.

To Sir Robert Robinson of Oxford University was presented the Society's Priestley Medal, highest honor in American chemistry. Sir Robert, Nobel Prize winner and internationally known authority on hormones and other natural chemicals, spoke on "Organic Chemistry at the Crossroads."

Professor Daniels also named the 1954 winners of ten other awards sponsored or administered by ACS. These awards will be presented at the Society's 125th national meeting to be held in Kansas City, Mo., March 24 through April 1. The recipients will be: *Garvan Medal*, Betty Sullivan, Vice-President and Director, Russell Miller Milling Company, Minneapolis; *American Chemical Society Award in Pure Chemistry*, John D. Roberts, California Institute of Technology; *Kendall Company Award in Colloid Chemistry*, Harry N. Holmes, Oberlin College; *Scientific Apparatus Makers Award in Chemical Education*,

Raymond E. Kirk, Polytechnic Institute of Brooklyn; *Eli Lilly and Company Award in Biological Chemistry*, Harvey A. Itano, California Institute of Technology; *Fritzsche Award* (essential oils), A. R. Penfold, Museum of Applied Arts and Sciences, Sydney, Australia; *Paul-Lewis Laboratories Award in Enzyme Chemistry*, Alton Meister, National Cancer Institute; *Fisher Award in Analytical Chemistry*, G. Frederick Smith, University of Illinois; *Borden Award in the Chemistry of Milk*, Donald V. Josephson, Pennsylvania State College; and *Precision Scientific Company Award in Petroleum Chemistry*, Arthur P. Lien, Standard Oil Company of Indiana.

An appeal for an early end to the government's atomic power monopoly was made by Harold C. Urey of the University of Chicago Institute for Nuclear Studies in a luncheon address during the meeting. He called for changes in the Atomic Energy Act to permit private companies to control the patents on their developments and to own fissionable materials and accessory substances. Warning that other nations may take the lead in industrial application of nuclear power unless the United States pays more attention to the problem, Professor Urey asserted that private enterprise offered the best hope of making the peacetime benefits of atomic energy available to the public. He predicted that real progress along this line would come through the efforts of new, small companies comparable to the Ford company of the automobile industry's early days, rather than through the activities of large concerns already in existence, which, he said, tend to regard atomic energy "as a nuisance of a competitor."

Discovery of a wide variety of nontherapeutic uses for antibiotics was reported. The conquest of halo blight, a disease causing vast losses in the nation's string-bean crop, has been achieved through the use of a streptomycin compound. Aureomycin ice has lengthened the storage life of freshly caught fish. Injection of cattle with antibiotics and other meat-curing substances has made meat more tender and flavorful and has improved its keeping quality. Antibiotics have been used to protect beer from contamination and to increase the alcohol yield from grain fermentation by curbing harmful bacteria. Evidence that antibiotics in feed accelerate animal growth by stimulating bone development also was presented.

Significant progress in attempts to develop chemical weapons against virus diseases was revealed by a panel of outstanding virologists at the first symposium ever held on viral chemotherapy. Although emphasizing that no compounds were as yet available for treating human patients, the participants told of several classes of chemical which have been found to halt or slow down the action of specific viruses in test tubes, in chick embryos, and in animals. The researchers expressed cautious optimism concerning the prospects of ultimately finding chemicals to control such diseases as polio, mumps, measles, and the common cold.

Advances in many other fields, including petroleum, paints, plastics, rubber, and nutrition also were reported in 1193 papers presented before the Society's 21 scientific and technical divisions.

WALTER J. MURPHY

American Chemical Society
Washington, D. C.

Science News

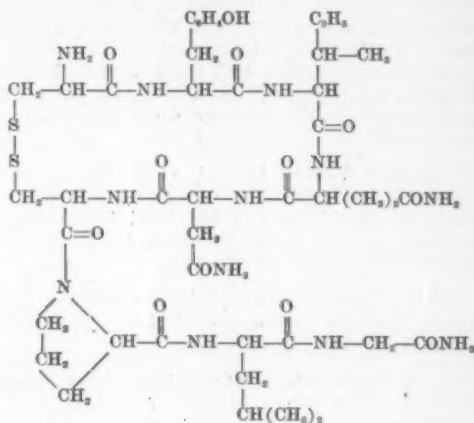
Stimulated by recorded observations that ancient Mediterranean armies were not as susceptible as modern armies to intestinal infections and that, further, the soldiers of the ancient armies drank wine heavily and usually under military orders, John Gardner, a student at the University of California, has conducted investigations to discover whether or not wine contains any antibacterial substances. He succeeded in isolating a substance which inhibits four representative bacteria. Although the inhibition is weak, the activity may be strengthened as the substance is further purified. For providing science with a new lead in its search for antibiotics, Mr. Gardner received the Kilmer Prize. This is awarded annually by the American Pharmaceutical Association to an undergraduate who has done outstanding independent research in pharmacy.

A compound which temporarily lowers blood pressure in animals has been isolated from rhododendron leaves by scientists of the National Heart Institute, U.S. Public Health Service. Although the compound, called andromedotoxin, has been obtained chemically pure, its structure is still unknown. It contains no nitrogen, yet resembles the veratrum alkaloids in physiological action. Small doses have a strong, brief hypotensive effect.

The work leading to this find has been carried out by two teams of scientists from the National Heart Institute. Over 1000 pounds of rhododendron leaves were required to make about 1 ounce of the chalk-white substance. The leaves came from West Virginia and North Carolina and were collected by the Department of Agriculture. Isolation procedures for obtaining the material from the source were conducted in Bethesda, Md., by Evan O. Horning, H. B. Wood, V. L. Stromberg, and J. C. Keresztesy. Pharmacological research with animals was done at Emory University School of Medicine by Neil C. Moran and A. P. Richardson. Dr. Moran recently reported on the work before the American Society for Pharmacology and Experimental Therapeutics. The drug has not been tested clinically.

It is announced in the *Journal of the American Chemical Society* (Oct. 5) that a group of scientists headed by Vincent du Vigneaud, Professor of Biochemistry at the Cornell University Medical College, has succeeded in synthesizing the pituitary hormone oxytocin, an important factor in childbirth and lacta-

tion. Working with Dr. du Vigneaud were Charlotte Ressler, John M. Swan, Carleton W. Roberts, Panayotis G. Katsouyannis, and Samuel Gordon. This is the first pituitary hormone, in fact the first polypeptide hormone, to be produced synthetically. It contains one equivalent each of 8 amino acids: leucine, isoleucine, proline, tyrosine, glutamic acid, aspartic acid, glycine, and cystine; and 3 equivalents of ammonia. It is a polypeptide with an approximate molecular weight of 1000, and as the following structural formula shows, is a cyclic disulfide.



The activity of the synthetic hormone has been assayed by the chicken depressor test. Its action on uterine muscle (isolated rat uterus and human uterus in labor) is as high as that of the natural hormone. It also has as high a milk-producing effect as natural oxytocin. One microgram injected intravenously will produce ejection of milk in 20 to 30 seconds.

The purified oxytocin has no effect on either blood pressure or the excretion of water by the kidney. There is a distinct hormone, vasopressin, with pressor and antidiuretic effects. Du Vigneaud and his co-workers, H. Claire Lawler and E. A. Popenoe, propose for vasopressin a structure similar to that of oxytocin, but with the leucine and isoleucine replaced by phenylalanine and arginine in beef vasopressin, and by phenylalanine and lysine in hog vasopressin. This indication that the same hormone obtained from different animals may have a different chemical structure is highly interesting.

The achievement of the synthesis of oxytocin, a name derived from the Greek word for rapid birth, establishes its chemical structure and thereby opens the door to many new investigations in biochemistry, pharmacology, and physiology. The synthesis may also provide an unlimited source of the oxytocic hormone for possible expansion of its use in clinical medicine, particularly in obstetrics and veterinary medicine.

Scientists in the News

Roger Adams, organic chemist and Head of the Department of Chemistry at the University of Illinois, has won the 1953 Midwest Award of the American Chemical Society's St. Louis Section. The award, an inscribed gold medallion, is presented annually in recognition of "meritorious contributions to the advancement of pure or applied chemistry or chemical research."

Joseph E. Alicata, Head of the Department of Parasitology, University of Hawaii Agricultural Experiment Station, has been given a leave of absence so that he might accept an assignment with the Division of International Health, U.S. Public Health Service, as Laboratory Director of Parasitology for the newly established Central Government Laboratory at Amman, Jordan.

Kurt Peter Anderko, formerly of the Max Planck Institut für Metallforschung of the Technische Hochschule, Stuttgart, has been appointed full research metallurgist at the Armour Research Foundation of the Illinois Institute of Technology.

Konrad Buettner has accepted the appointment of Acting Associate Professor of Meteorology at the University of Washington, Seattle.

Marion T. Clark, Assistant and Acting Chairman of the University Relations Division of the Oak Ridge Institute of Nuclear Studies for the past 2½ years, has returned to Emory University to resume his post as Associate Professor of Chemistry.

Vining C. Dunlap, Director of Tropical Research for the United Fruit Company, has retired after 31 years of service. In August the company's new Vining C. Dunlap Laboratory for Tropical Research in La Lima, Honduras, was dedicated in Dr. Dunlap's honor.

W. E. Edington, formerly Head of the Department of Mathematics at DePauw University, has been made Professor Emeritus.

John D. Ferry of the University of Wisconsin has been presented the 1953 Bingham Medal in recognition of his outstanding contributions to rheology.

On September 16 the President announced the recess appointment of **Laurence McKinley Gould**, President of Carleton College, Northfield, Minnesota, and leading geologist and geographer, to the National Science Board of the National Science Foundation. Dr. Gould will fill out the term of **James B. Conant** which expires May 10, 1956. Dr. Conant resigned when he became U.S. High Commissioner for Germany. The National Science Board is the primary policy-making body of the National Science Foundation.

David B. Hand, head of the Division of Food Science and Technology, New York State Agricultural Experiment Station, Geneva, has been granted six months' leave of absence by Cornell University to make a

survey of food processing on Formosa. He will be a member of the technical staff of The J. G. White Engineering Corporation of New York City, consultants to the National Government of the Republic of China. The project is being financed by the U.S. Foreign Operations Administration.

Thomas Little, assistant professor of biology who resigned from the University of Nevada in protest over the dismissal of Frank Richardson (News and Notes, Aug. 7), has been appointed an associate agriculturist for the University of California. His headquarters are at Riverside, where he will act as farm advisor to the agricultural extension work for ten Southern California counties.

Alfred O. C. Nier, physicist at the University of Minnesota, has succeeded **J. W. Buchta** as Head of the Physics Department. Dr. Buchta, department chairman for 15 years, has been appointed Associate Dean of the College of Science, Literature and the Arts. The first scientist to isolate Uranium-235, Dr. Nier has played a vital role in the development of fundamental knowledge about atomic energy.

Frank Press, Associate Professor of Geology at Columbia University, has accepted a 3-month appointment to the UNESCO program of technical assistant to Israel. Dr. Press will return in December, when he will have completed supervising the installation of two seismograph stations and training personnel in their operation.

Frederick G. Sawyer, former Assistant to the Director of Research at Stanford Research Institute, has recently joined The Ralph M. Parsons Company, Los Angeles, where he is engaged in special projects in the fields of chemical and petroleum engineering.

Marshall R. Warren, Associate Professor of Pharmacology at the University of Tennessee Medical Units, has resigned to accept a position as Chief of the Division of Pharmacology in the research laboratory of Mead Johnson, Evansville, Ind.

On the anniversary of his 70th birthday last spring, **Carl J. Wiggers** was the recipient of the honorary degree of Doctor of Medicine honoris causa, from the Medical Faculty of the Ludwig-Maximilian University, Munich, Germany. Dr. Wiggers was a pupil of Otto Frank in the Physiological Institute of that university in 1912.

Dr. Wiggers became an Emeritus Professor of Physiology from Western Reserve University after 35 years of service. He is now Honorary Professor of Physiology in the Frank E. Bunts Educational Institute associated with the Cleveland Clinic.

Jerome J. Wolken has recently been appointed Director of Research for the Eye Bank of Pittsburgh and also head of a new biophysics research laboratory at the Eye and Ear Hospital, University of Pittsburgh Medical Center. He will study photosynthesis, photoreceptors, and photobiology.

Education

Establishment of a new research unit at **Columbia University** has been announced jointly by the university and the Daniel and Florence Guggenheim Foundation, which has provided a grant of \$329,000. The new unit will be known as the **Daniel and Florence Guggenheim Institute of Air Flight Structures**. Preliminary organizational steps are proceeding, and the new Institute will begin operation on Jan. 1, 1954. Its activities will be carried out by the Department of Civil Engineering, and by other appropriate segments of the university working closely with Civil Engineering.

An advisory board consisting of aviation and engineering experts will be appointed to assist in guiding the Institute's activities. The purposes of the new unit are: to train exceptionally qualified graduate students in the comparatively new field of air flight structures; to conduct research in aircraft structure and design, especially for supersonic flight; to act as a national clearinghouse for technical information in this field; and to disseminate technical knowledge regarding air flight structures.

The Division of Geological Sciences at **Harvard University** has a new building, a modern two-story masonry addition to Dunbar Laboratory in which experimental programs under the direction of Francis Birch, Sturgis Hooper Professor of Geology, will be housed, together with shop facilities formerly located in another building.

A series of eight monthly lectures is being offered at the **Illinois Institute of Technology** for high school science teachers to keep them informed of the latest developments in their fields. The schedule calls for two lectures each in the fields of chemistry, physics, biology, and mathematics. Teachers are encouraged to bring guests; there is no charge for admission.

A revised curriculum is now in effect for entering students at the **Massachusetts Institute of Technology**. For the first time in the Institute's history most freshmen registering this fall were able to choose one elective course, in addition to four subjects and the basic military science course required of all entering students. These electives range through many areas, from spoken languages to the theory of numbers. Several "survey courses," intended to introduce students to basic principles in broad areas of scientific interest, are being given for the first time. Among these are Elementary Meteorology, Perspectives in Life Science, Conservation of Natural Resources, and Earth Science.

Recent statistics about MIT are of general interest. The combined academic and research budgets during 1952-53 came to nearly \$43,000,000—a sum almost equalling the peak reached during World War II. The students, staff, and other personnel which make up the MIT community exceeded 11,000, the largest number to date. There were 5074 students,

3154 of them undergraduate. The enrollment of graduate students, 1921, was a new high. Further, in 1953-54 MIT will have 63 National Science Foundation fellows, or 11% of all those selected for the entire country.

Grants and Fellowships

Yale University and the **Bernice P. Bishop Museum** of Honolulu are offering a series of **Bishop Museum Fellowships** for scientific research in the Pacific, two of which are awarded annually. Similar fellowships were awarded prior to World War II.

The first fellowship in the new program has been awarded to Frank Richardson of Reno, Nevada, former Chairman of the Department of Biology of the University of Nevada (News and Notes, Aug. 7). Dr. Richardson will conduct a program of research on the breeding cycles of sea birds in the Hawaiian Islands. He has arrived in Hawaii and has commenced his field observations. Dr. Richardson's headquarters are established at the Bishop Museum.

Nominations are now being received by the American Pharmaceutical Association for the 1954 **Chilean Iodine Education Bureau Award** recognizing outstanding research in the chemistry and pharmacy of iodine and its compounds as applied in pharmacy or medicine. The award consists of \$1,000 and a diploma setting forth the reasons for selection of the recipient. It may be presented each year at the annual meeting of the Association.

Any member of the Association may propose a nominee by submitting eight copies of each of the publications to be considered in the competition, a biographical sketch of the nominee including date of birth, and a list of his publications. Eight copies of the nomination must be submitted to Robert P. Fischelis, Sec., American Pharmaceutical Association, 2215 Constitution Ave., N.W., Washington 7, D.C. *Nominations must be received on or before Jan. 1, 1954.*

A nominee must be a resident of the United States or Canada. He must have accomplished outstanding research in the chemistry or pharmacy of iodine and its compounds as applied in pharmacy or medicine.

The Department of Meteorology at **Florida State University**, Tallahassee, announces the availability of graduate assistantships for qualified students. The assistantships are in connection with the department's research activities, supported in part by contracts with the Geophysics Research Directorate, Air Force Cambridge Research Center, and the Geophysics Branch, Office of Naval Research.

The minimum stipend is \$1,620 per year plus waiver of out-of-state tuition for students who hold a bachelor's degree from an accredited institution and have completed at least one year of university physics and one year of calculus. The minimum stipend is \$1,920 per year plus waiver of out-of-state tuition for students who hold an M.S. degree in meteorology. Gradu-

ate assistants are permitted to carry as many as ten semester hours of course work.

Application blanks and additional information may be obtained by writing Dr. Werner A. Baum, Head, Department of Meteorology, Florida State University, Tallahassee, Florida. *Applications for 1954-55 should reach the Department of Meteorology before March 31, 1954; however, all possible consideration will be given to applications that arrive at a later date.*

The National Heart Institute of the U.S. Public Health Service is conducting a research training program in enzyme chemistry at the Institute for Enzyme Research of the University of Wisconsin. Candidates must possess a Ph.D. or M.D. degree. Stipends conform to those in effect for postdoctorate research fellows of the Public Health Service. The period of training is 12 months.

Application forms and further information may be obtained from Dr. D. E. Green, Institute for Enzyme Research, Madison, Wis. *Applications should be submitted preferably before Jan. 15, 1954.*

Northwestern University has announced receipt of a \$6000 grant from the United Cerebral Palsy Association of Chicago. The gift is for support of research on the speech development of children with cerebral palsy under the direction of Harold Westlake of the speech clinic.

The School of Graduate Studies, Michigan State College, offers the following appointments to qualified students, predoctoral and postdoctoral. Inquiry should be directed to the Dean, School of Graduate Studies, Michigan State College, East Lansing, unless other directions are given.

Graduate Assistantships. Stipends range from \$1,000 to \$1,400, with a few at higher values, depending upon the nature and extent of service required. Direct inquiries to the appropriate department heads.

Tuition Scholarships. These appointments carry remission of fees and, in the cases of some foreign students, an additional award of \$75.00 per quarter.

Predocctoral Fellowships. About twenty such appointments are made each year. Stipends range from \$500 to \$1,200, and in most but not all cases fees are waived. No service to the College is required.

Postdoctoral Fellowships. One of these, carrying a stipend of \$3,000, is awarded each year for research in a field for which the college has appropriate facilities.

The Social Science Research Council has announced that the following fellowships and grants are being offered in 1954. The awards are of two distinct types:

(1) Those designed exclusively to afford training in research in social science. These include the Research Training Fellowships and Undergraduate Research Stipends.

(2) Those designed to aid scholars of established competence in the execution of their research, namely, the Faculty Research Fellowships and Grants-in-Aid of Research. The latter do not provide full maintenance,

and are not available to students working for degrees.

No funds are available for subsidizing the publication of books or articles. All awards are restricted to permanent residents of the United States or Canada. Faculty Research Fellowships are offered only in the United States. *Applications, on forms provided by the Council, must be filed not later than Jan. 4, 1954.* Inquiries, which should indicate age, academic status, vocational aims, the nature of the proposed training or research, and the type of assistance desired, should be addressed to the Washington office of the Council at 726 Jackson Place, N.W., Washington 6, D.C.

Meetings and Elections

The 2nd Conference of Industrial Hygiene in Yugoslavia, organized by the Institute of Industrial Hygiene, Yugoslav Academy of Sciences and Arts, was held in Zagreb, Sept. 6-9. The conference gained a more than purely regional importance by the participation of research workers from 9 other countries. In the section on toxicology the emphasis was placed on poisoning with heavy metals, especially lead, which remains one of the pressing problems of occupational medicine in Yugoslavia. Numerous reports were concerned with the psychology and physiology of human work. As an experiment in international scientific cooperation, the abstracts of all the papers, irrespective of the language in which the report was actually presented, were made available in printed form both in Croatian and in English.

An international Cosmic Ray Conference sponsored by the National Science Foundation and Duke University will be held on the Duke Campus Nov. 30-Dec. 2. Some 60 to 70 leading physicists will take part in the meeting, designed to evaluate the current status of cosmic ray research. Among the group will be scientists from France, England, Sweden, Mexico, Canada, Puerto Rico, Bolivia, and Brazil, as well as from the United States.

The main emphasis of the conference will be on high-energy phenomena which are beyond the range of present-day accelerators. During 6 sessions in the 3-day meeting, the scientists will present 40 or more invited papers on such topics as the origin, time, fluctuations, and propagation of cosmic rays, new unstable particles, and nuclear interactions.

The conference committee will consist of Prof. B. Rossi, Massachusetts Institute of Technology, chairman; Prof. C. Anderson, California Institute of Technology; Prof. M. Schein, University of Chicago; Dr. R. J. Seeger, National Science Foundation; and Dr. L. W. Nordheim, Duke University.

A meeting of importance to industrial health activities will be held by the Industrial Hygiene Foundation on Nov. 18 and 19 at its headquarters at the Mellon Institute, Pittsburgh. Some 600 management executives, physicians, engineers, toxicologists, chemists, attorneys, and industrial hygienists will attend this

18th annual meeting. More than 40 authorities will address the representatives of the 360 member companies of the Foundation. They will present new material in the field of industrial health, and will lead discussions that afford a valuable exchange of information on specific problems encountered in a wide variety of industries.

The Interamerican Society of Psychology (sIp) has been invited by the Dominican Republic to celebrate its first meeting from Dec. 10 to 20 at the University of Santo Domingo, the oldest University of the Americas. Sixty delegates from all of the American countries, among them 15 representatives of the United States and Canada, will be guests at the Hotel Jaragua in Ciudad Trujillo.

There will be 5 general inter-American round-table discussions: (1) tasks and limits of psychological disciplines; (2) the professional and legal situation of the psychologist; (3) the present state of psychology in the various countries of the Americas; (4) psychology of culture and of values; and (5) controversial problems of psychology, education, and psychiatry. Delegates will be asked to present papers which will be published. Applications of citizens of the United States and Canada for membership in the sIp should be sent, accompanied by a curriculum vitae in triplicate, to Werner Wolff, vice president of the sIp, Dept. of Psychology, Bard College, Annandale-on-Hudson, N.Y.

During the 19th International Physiological Congress at Montreal a meeting open to all pharmacologists attending the Congress was held at McGill University. At this meeting, it was decided to set up a council of seven members from seven different nations, to look after the interests of pharmacologists in future international congresses, to explore the possibility and desirability of affiliating with the newly formed International Union of Physiological Sciences, to collect and distribute information about the activities of pharmacological organizations, and to perform such other functions as might seem necessary and advisable. The following council members were elected: Daniel Bovet, Italy; J. H. Burn, England; C. Heymans, Belgium; K. O. Möller, Denmark; E. Rothlin, Switzerland; C. F. Schmidt, USA; and H. Weese, Germany. This council subsequently selected Dr. Heymans as president, Dr. Schmidt as secretary, and adopted the name International Council of Pharmacologists.

The Mycological Society of America has elected the following officers for 1953-54: pres., Leland Shanor, University of Illinois; v. pres., Donald P. Rogers, New York Botanical Garden; sec.-treas., C. J. Alexopoulos, Michigan State College (for 3-year term). Representatives to the AAAS Council are Wesley G. Hutchinson, Laboratory of Microbiology, University of Pennsylvania and Grant D. Darker, Ben Venue Laboratories, Bedford, Ohio. William W. Diehl, Division of Mycology, Plant Industry Station, Beltsville,

Md., has been appointed to replace Dr. Hutchinson on the Council beginning Jan. 1, 1954.

The National Shellfisheries Association has elected the following officers for 1953-54: pres., A. F. Chestnut, Institute of Fisheries Research, Moorhead City, N.C.; v. pres., G. Francis Beaven, Chesapeake Biological Laboratory, Solomons, Md.; sec.-treas., M. R. Carriker, Dept. of Zoology, Rutgers University.

The Texas Academy of Science will hold its annual meeting, as guests of the Medical Branch of the University of Texas at Galveston on Dec. 3-5. The Collegiate Division and the Junior Academy will meet with the Senior Section.

Miscellaneous

Recent visitors from abroad at the National Bureau of Standards:

Severino Parientes, Sales Manager, Clay Products Company, Panama.

Frederic G. Foster, Statistician, University of London, London, England.

Masashi Homma, Professor, Department of Civil Engineering, Tokyo University, Tokyo, Japan.

Fojiro Ishihara, Professor, Civil Engineering Department, Kyoto University, Kyoto, Japan.

H. J. Schoemaker, Associate Director, Hydraulic Laboratory, Delft, The Netherlands.

Umberto Colombo, Research Chemist, Montecatini Chemical Company, Nonara, Italy.

Wilfred Abson, Harwell Laboratory, Harwell, England.

Denis Taylor, Director of Electronic Division, Harwell Laboratory, Harwell, England.

Toshimitsu Murasaki, Instructor in Aeronautics, Tokyo University, Tokyo, Japan.

Evert Aulin, Aktiebolaget Gas Accumulator, Lidö, Sweden.

Maurice V. Wilkes, Director, The University Mathematical Laboratory, University of Cambridge, Cambridge, England.

D. I. Lawson, Assistant Director, Fire Research Station, Department of Scientific and Industrial Research, Hertz, England.

Rolando Salvadorini, Research Laboratory, Radio Italiana, Torino, Italy.

Ikhtiar-ul-Mulk, Chief Research Officer, Government of Pakistan, Karachi.

Saburo Muroga, Research Engineer, Nippon Telephone and Telegraph Corporation, Tokyo, Japan.

Chujoe Yamanaka, Osaka University, Osaka, Japan.

Jamshed Maneshka, Deputy Director of the India Supply Mission, Lahore, Pakistan.

Erratum: In News and Notes, Sept. 25, there was an error in the listing of the officers of The Kansas Academy of Science. D. J. Ameel, Head of the Department of Zoology, Kansas State College, is vice president, and C. A. Rogerson, Assistant Professor of Botany, Kansas State College, is secretary.

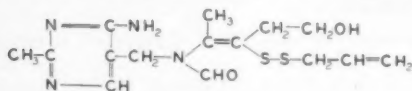
Technical Papers

The Effects of Allithiamine on Some Thiamine-Requiring Organisms¹

Virgil Greene Lilly, H. L. Barnett,
and B. G. Anderson²

Department of Plant Pathology, Bacteriology,
and Entomology, and Department of Biology,
West Virginia University, Morgantown

Matsukawa and Yurugi (1) prepared allithiamine by reacting thiamine with allicin under mild alkaline conditions. Fujiwara and Watanabe (2) found allithiamine to replace thiamine for rice birds and the rat. The structure of allithiamine is shown below:



Experiments with thiamine-requiring fungi. The value of allithiamine as a replacement for thiamine was determined for 5 thiamine-requiring fungi: *Endoconidiophora fimbriata*, *Mucor ramannianus*, *Phycomyces blakesleeanus*, *Schizothecium longicolle*, and *Thielaviopsis basicola*. Suboptimal amounts of allithiamine and thiamine chloride hydrochloride were added to a thiamine-free glucose asparagine medium. The cultures were incubated at 25°. The techniques used are described by Lilly and Barnett (3). The amount of growth was determined by harvesting and weighing the dry mycelium.

Allithiamine and thiamine were sterilized in 3 ways: (a) by autoclaving with the basal medium, (b) by autoclaving dilute distilled water solutions, and (c) by filtering dilute distilled water solutions using Pyrex sintered glass bacteriological filters. The activity of thiamine for the 5 test fungi was almost completely lost when thiamine was autoclaved in distilled water; the activity of allithiamine was not changed by this treatment.

On a weight basis, allithiamine was more active than thiamine for *E. fimbriata*, *M. ramannianus*, and *P. blakesleeanus*; and less active for *S. longicolle* and *T. basicola*. This was confirmed in repeated experiments. The results from a typical experiment for 2 fungi are shown in Fig. 1.

In view of the ready conversion of allithiamine into thiamine, when treated with cysteine, and the similarity of allithiamine and thiamine disulfide, it ap-

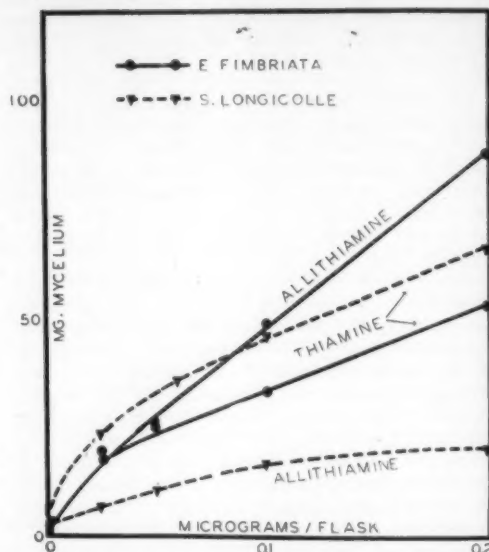


FIG. 1. Growth of *E. fimbriata* (11 days) and *S. longicolle* (14 days) on various concentrations of allithiamine and thiamine.

pears probable that fungi convert allithiamine into thiamine. This hypothesis was tested in the following way. *P. blakesleeanus* was grown on media containing 100 µg each of allithiamine and thiamine. The mycelium was harvested, washed, and dried at 50°. The 2 samples of mycelium were used as sources of thia-

TABLE 1
MILLIGRAMS OF DRY MYCELIUM PRODUCED BY 5 TEST FUNGI WHEN THE BASAL MEDIUM CONTAINED 15 MG OF *P. blakesleeanus* MYCELIUM GROWN ON ALLITHIAMINE AND THIAMINE. CONTROLS WERE GROWN IN THE PRESENCE OF 0.1 µg OF ALLITHIAMINE AND THIAMINE

Species	Days of incubation	Alli-thia-mine-mycelium	Thia-mine-mycelium	Alli-thia-mine	Thia-mine
<i>E. fimbriata</i>	11	44	46	49	33
<i>M. ramannianus</i>	9			33	21
	11	30	29		
<i>P. blakesleeanus</i>	7	43	33		
	8			66	49
<i>S. longicolle</i>	12	40	44		
	14			17	46
<i>T. basicola</i>	11			17	32
	12	38	32		

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² We wish to thank Saburo Fukui and Montonori Fujiwara of Kyoto University, who supplied the allithiamine used. We are indebted to John B. Conn of Merck & Company, Inc., who furnished an analytically pure sample of thiamine chloride hydrochloride. Our especial thanks are due to Mrs. Betsy Morris Waters, who carried out many of the experiments with the fungi.

mine (or allithiamine) for 5 test organisms. Some of these results are reported in Table 1. The yields obtained with 0.1 μ g of allithiamine and thiamine are included for the purpose of comparison.

Aqueous extracts, prepared from the allithiamine and thiamine-mycelium were treated with alkaline ferricyanide and cyanogen bromide. The thiamine activity of the treated extracts was destroyed equally for 2 test fungi: *E. fimbriata* and *P. blakesleeana*. Since control experiments under the same conditions had shown that thiamine was inactivated while the activity of allithiamine was only slightly diminished, it was concluded that allithiamine is converted into thiamine by *P. blakesleeana*.

Experiments with albino rats. Four weanling albino rats were fed a thiamine-free diet until two of them died. At that time, the 2 surviving rats were transferred to a diet containing allithiamine, but otherwise the same as the thiamine-free diet. After 2 wk on allithiamine, they were placed on a diet containing thiamine instead of allithiamine. The results for both rats were essentially the same. Figure 2 shows the results

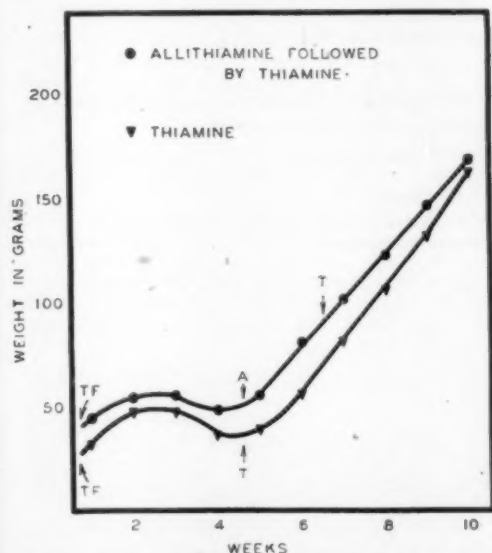


FIG. 2. Growth curves for 2 male rats kept on the thiamine-free diet for 4 wk, followed by allithiamine for 2 wk for 1 rat (circles) and by thiamine for the other (triangles). Time of change of diet is indicated by arrows: TF, thiamine-free diet; A, thiamine-free diet plus allithiamine; and T, thiamine-free diet plus thiamine.

for 1 of the 2 rats. Note that, after being placed on the thiamine-free diet, the rat gained weight during the 1st and 2nd wk, leveled off during the 3rd wk, and lost during the 4th wk. When transferred to the allithiamine diet, the rat gained rapidly and continued to gain after being transferred to the thiamine diet. For comparison, a typical growth curve for another rat from a series of experiments in which the rats were

changed from the thiamine-free diet directly to the thiamine diet is also shown. On the basis of the above results, one may conclude that allithiamine may replace thiamine in the diet of the rat.

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The Effect of Cortisone upon the Therapeutic Efficacy of Antibiotics¹

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It is well established that cortisone enhances various infections in animals and man and aggravates their severity (1). This property is attributable to a depression of the antimicrobial defenses of the host, rather than to a direct promotion of microbial growth or invasiveness (2). To protect a patient receiving cortisone against dissemination of latent or active infection, antibiotics are often administered. The question arises whether cortisone might also impair the therapeutic effectiveness of antimicrobial agents. If certain of these drugs acted in conjunction with normal antimicrobial defenses of the host then the depression of these defenses by cortisone might result in measurable impairment of the curative effect of these drugs. The experiments reported here were undertaken to explore this possibility.

The following laboratory model was used. White Swiss mice (15-19 g) were infected intramuscularly with a virulent strain of *Klebsiella pneumoniae*. The LD₅₀ of this strain consisted of 50-100 organisms injected into the thigh muscle, in a volume of 0.1 ml. After infection with 10-500 LD₅₀, all animals died in 3-5 days with positive heart blood cultures. The antibiotics, aureomycin hydrochloride² and streptomycin sulfate were dissolved in suitable concentration in saline, and each dose was administered intraperitoneally in a volume of 0.2 ml. Antibiotic treatment was started 6 hr after infection, two doses were administered on the next day, and a single daily dose on the following 3 days.

Cortisone acetate was suspended in saline and a daily subcutaneous dose of 10 mg/kg was administered for 5 consecutive days, beginning 24 hr before infection. This dose of cortisone was not harmful to the animals (3) and permitted normal growth and weight gain. Alternate groups of mice received cortisone as shown in Table 1.

¹ Supported by a grant (E214) from the National Institutes of Health, U.S. Public Health Service.

² Supplies of aureomycin hydrochloride were made available by Dr. Stanton Hardy, Lederle Laboratories.

TABLE 1
IMPAIRMENT OF ANTIBIOTIC EFFECTIVENESS
BY CORTISONE

No. of <i>Klebsiella pneumoniae</i> injected intramuscularly	Antibiotic		Cortisone total dose, mg†	Mortality of mice		P‡
	Drug	Dose, mg*		Dead/total	Per cent	
20,000	Aureomycin	0.5	0	25/25	100	—
20,000	Aureomycin	0.5	1.0	25/25	100	—
20,000	Aureomycin	1.0	0	17/25	68	0.03
20,000	Aureomycin	1.0	1.0	24/25	96	—
20,000	Aureomycin	2.0	0	3/25	12	0.005
20,000	Aureomycin	2.0	1.0	18/25	72	—
20,000	Aureomycin	4.0	0	0/25	0	0.05
20,000	Aureomycin	4.0	1.0	5/25	20	—
1000	Aureomycin	1.0	0	2/24	8	0.001
1000	Aureomycin	1.0	0.75	16/25	64	—
1000	Aureomycin	2.0	0	1/20	5	—
1000	Aureomycin	2.0	0.75	1/24	4	—
50,000	Streptomycin	0.06	0	24/30	80	0.1
50,000	Streptomycin	0.06	0.75	29/30	97	—
50,000	Streptomycin	0.18	0	1/30	3	0.009
50,000	Streptomycin	0.18	0.75	10/30	33	—
50,000	Streptomycin	0.6	0	0/29	0	—
50,000	Streptomycin	0.6	0.75	0/30	0	—
1000	—	—	—	48/48	100	—
—	—	—	1.0	1/46	2	—
—	—	—	0.75	0/54	0	—

* Injected intraperitoneally in 5 equal doses, beginning 6 hr after infection.

† Injected subcutaneously in 5 equal, daily doses, beginning 24 hr before infection.

‡ Probability of chance occurrence estimated by chi-square test. A figure of 0.05 or less indicates statistical significance of the difference.

Groups of 25–40 mice were infected and treated with various dosage levels of antibiotic. The animals were carefully observed for the development of the local lesion in the thigh which always preceded the systemic illness and death. Deaths and survival times were recorded and the differences in mortality rates subjected to the chi-square test for determination of statistical significance. The results of representative experiments are summarized in Table 1.

The single death among 46 control mice receiving 1.0 mg of cortisone must be attributed to an accident: there was no evidence of infection or gross abnormality. The average survival time of infected animals with and without cortisone did not differ significantly.

The antibiotic doses were so adjusted as to cover a range from complete protection to none. It can be seen from Table 1 that over much of this range the cortisone treatment of animals materially depressed the rate of cure which could be achieved with any given dose of the antibiotic. This interference with the curative effects of the antibiotic applied not only to the bacteriostatic drug, aureomycin, but also to the bactericidal drug, streptomycin. Other experiments, to be reported elsewhere, revealed similar effects of cortisone in a variety of bacterial infections treated with a

number of antibiotic agents. In all instances a large excess of the antibiotic drug overcame this effect of cortisone and resulted in cure in spite of cortisone administration.

These experiments suggest that defenses of the host may materially aid the direct antimicrobial action of antibiotics (4–6). When cortisone depresses these host mechanisms, the manifest outcome appears to be an impairment of the therapeutic effect of the antibiotic. This observable end result is most pronounced with barely curative amounts of the antibiotic. With much larger doses of antibiotic the contribution of host defenses in overcoming the infection is less essential and consequently the cortisone effect is not readily demonstrable. The mechanism of these contributory host defenses is currently under study.

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Resumption of Heartbeat in the Rabbit Embryo after Exposure to Low Temperatures¹

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Since the discovery of glycerol as a protective agent for the vitrification of spermatozoa at low temperature by Polge, Smith, and Parkes (1), deep-frozen bull semen has been successfully used in artificial insemination (2). Revival of mammalian ovarian tissue (3), revival of chick heart, and development of the chick embryo (4–6) after deep freezing have been reported. This paper reports a series of preliminary experiments on the resumption of the heartbeat in early rabbit embryos after exposure to various low temperatures.

Ten-day-old rabbit embryos were removed from the uteri under a stereoscopic microscope. Equal volumes of buffered Locke-Ringer solution and rabbit serum were used as a medium for the embryos before treatment and for their culture in Carrel flasks after treatment.

For treatment at 10° or at 0° C, the embryo was placed in a Carrel flask containing 5 ml of serum-Ringer fluid and kept either in a constant temperature bath at 10° C or in a Thermo flask containing ice for 1 day. After storage, the flask was attached to a rocking device (7) in an incubator at 38° C.

¹ This work was supported by grants from the Rockefeller Foundation and the Dickinson Memorial Fund of the Planned Parenthood Federation. Thanks are due to Elizabeth M. Hull for assistance.

The media prepared for treatment of embryos at still lower temperatures were 5, 10, and 15% glycerol in serum-Ringer fluid. The embryos were suspended consecutively in these solutions for 10-20 min each, at a temperature of about 32° C. One or two embryos then were placed in a small Pyrex tube containing 15% glycerol and stoppered with a rubber bulb. For cooling at -10° C, the tube was kept at 10° C for 1 hr, 0° C for 1 hr, and then was transferred into a Thermos flask containing a freezing mixture (solid CO₂ in acetone and 95% alcohol) adjusted to -10° C for 1-2 hr. The embryos were then transferred into a Carrel flask for culture.

For deep-freezing at -75° C, cooling at different rates was performed as follows. For fast cooling, the tubes containing embryos at room temperature (20-25° C) were placed directly into a deep-freezing mixture at -75° to -79° C. This cooling took place in less than 1 min. For medium cooling, the deep-freezing apparatus devised by Polge and Lovelock (8) was used. Cooling from 20° to 0° C took place in about 15 min and from 0° to -75° C in about 30 min. For slow cooling, the tubes containing embryos were first placed in a bath at 10° C for 1-10 hr and then transferred into ice for 1-10 hr. The tubes were then placed either into the deep-freezing apparatus when its temperature was 0° C, and allowed to drop to -75° C, or into a freezing mixture at 0° C to which solid CO₂ was added gradually until the temperature dropped to -75° C, in 30-60 min. The tubes were kept at -75° C for 10-80 min and then transferred into a water bath at 40° C. Thawing took place in about 1 min. The embryos were transferred and cultured in Carrel flasks containing serum-Ringer fluid. Examinations by means of different magnifications under stereoscopic or compound microscopes were performed approximately every 6-12 hr during culture, and the number of heartbeats/minute was recorded.

From the summary of results in Table 1 it is evident that early rabbit embryos can resume their heartbeat after exposure to low temperatures, although the effects of different temperatures on the embryos may vary. After exposure to temperatures of +10° to -10° C for various lengths of time, the appearance of the embryos was quite normal. Resumption of the heartbeat occurred after from a few minutes to 2-4 hr in culture. Rhythmic contractions of the atrium and ventricle were obvious, though the rate dropped and irregularity of the beat (i.e., contractions of the bulb, atrium, and ventricle not in pace) occurred at the end of culture.

After the treatment at -75° C, before culture, the embryos appeared shrunken but otherwise normal. In culture, they did not recover their normal size and contractions of the heart region were observed only after 12-24 hr. Certain anatomical structures such as the somites, brain vesicles, ear and eye cups, and the different parts of the heart became indistinct, and in some cases the whole embryos appeared like masses of tissue. Although rhythmic contractions of the bulbar region in the inner part of the heart were observed

TABLE 1
RESUMPTION OF THE HEARTBEAT IN RABBIT EMBRYOS
AFTER EXPOSURE TO LOW TEMPERATURES

Treatment of embryos	No. of embryos tested	No. of embryos which resumed heartbeat	Remarks on the embryos which resumed heartbeat*	
			Initial beats/min in culture	Beats/min after culture
No treatment, cultured at 38° C	7	6	80-96	19-52 after 1-3 days
At 10° C for 1 day	9	5	25-55	12-62 after 1-1.5 days
At 0° C for 1 day	9	5	35-70	18-82 after 1-1.5 days
At -10° C for 1-2 hr	3	3	42-88	38-72 after 1-1.5 days
At -75° C for 10-80 min	6	1		47 after 1 day under compound microscope
Fast cooling				
Medium cooling	18	5	57 (one embryo)	37-63 after 1 day: observed in 1 embryo under 32X and in 4 embryos under 72X
Slow cooling	16	5		35-55 after 1 day: observed in 5 embryos under 72X

* Individual embryos were cultured for various lengths of time. The range of these times and the range of beats/min are presented. In the series treated at -75° C, the heartbeat was recorded only after culture in most cases.

in the majority of the embryos that resumed their heart contraction, in only one embryo, after medium cooling, were contractions of the bulb and atrium observed.

Throughout this study, it was noticed that not all the embryos could resume their heartbeat even under the most favorable conditions, e.g., in culture. However, some were able to maintain their heartbeat for 2 to 3 days in culture, even though they underwent no obvious further development. In 10-15% glycerol at 32° C, the heartbeat of some embryos was observed, but only for a short time (1-2 hr). In 20-25% glycerol, it was observed for no longer than 5 min. Various percentages of ethylene glycol and glycerol with Cellosolve were tested, but no advantage was noticed. A few tests indicate that 10-day embryos can withstand low temperatures better than 11-13-day embryos.

The rate of cooling, especially to -75° C, may play an important role in the subsequent resumption of the heartbeat in rabbit embryos, although in the present study, no striking difference in effect was revealed between the medium and slow rates of cooling. It appears that the effects of different temperatures on the dif-

ferent tissues vary. Growth of chorionic tissue was observed in every case and contractions of the heart region were observed in a few instances. However, distortion of the brain vesicles and eye cups was observed in every case after deep-freezing. It seems, then, that tissue of mesodermal origin may withstand deep-freezing better than that of ectodermal origin.

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Lack of Protective Effect of Allyl Thiourea Against X-Irradiation¹

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Alexander and Fox (1) recently found a correlation between the ability of various agents to protect animals against x-rays and the ability of these agents to protect polymethacrylic acid from radiation-induced loss of viscosity. The most effective agent they tested in their polymer system was allyl thiourea, and they pointed out that this chemical had never been tested biologically.

We have found that allyl thiourea does not protect

TABLE 1
EFFECT OF ALLYL THIOUREA ON LETHALITY OF WHOLE BODY X-RADIATION TO MICE*

Expt.	Allyl thiourea (mg/kg)	X-rays (r)	Lethality	Average length of survival (days)
1	0	800	16/16	11.9
	250	0	0/16	—
	250	800	16/16	8.9
2	0	750	16/16	10.3
	35	750	16/16	7.0
	100	750	16/16	9.6
	250	750	16/16	10.7
	250	0	0/16	—

* Mice were Carworth Farm males, age approximately 60 days. Allyl thiourea freshly prepared for each use and injected within 15 min before beginning x-radiation. X-Ray factors: 250 KVP, 15 ma, 1/4 mm Cu + 1 mm Al, 60 cm target distance. Rate: 60 r/min in expt. 1; 53 r/min in expt. 2. Lethality is expressed as the number of deaths over the total number tested.

¹ This study was supported by funds provided under contract AF 33(038)27353 with the USAF School of Aviation Medicine, Randolph Field, Texas.

mice from the lethal effects of whole body x-irradiation, and it therefore appears that the interesting polymer system of Alexander and Fox may not be used as an *in vitro* test of *in vivo* protective action.

Allyl thiourea is relatively nontoxic and soluble and may be given intraperitoneally to mice at a dose rate of 250 mg/kg without effect. In the experiments reported here we administered 750 or 800 roentgens of whole body x-radiation to our mice; these doses are 100% fatal, but appreciable percentages of mice may be saved from these doses by sodium azide, cysteine, or other agents shown by Alexander and Fox to be less effective than allyl thiourea in their polymer test system.

The results of two experiments are given in Table 1, which indicate no protective effect whatsoever of allyl thiourea. In fact, in some cases the drug, though without toxicity itself, seems to hasten the lethal result of the x-radiations.

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Photoperiodic Behavior of Medium-Early Varieties of Rice

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The effect of short days of 10 hr (8:00 A.M.-6:00 P.M.) on the flowering behavior of medium-early rice (1) has been studied. Three varieties, T.3 (a selection from Basamati of Dehradun), T.12 (a selection from Hansraj of Unnab district), and T.21 (a selection from Chawal of Rampur State), grown in Uttar Pradesh, were used in pot-culture experiments. Pure seeds of these varieties, obtained from Nagina Rice Research Station, U.P., after a preliminary selection for uniformity by eye, were sterilized in 0.2% formalin, thoroughly washed in distilled water, and sown on June 18, 1949. Germination was complete in 5-6 days. Short-day treatment² was started in the seed bed with 7-day-old seedlings. Short days were given for periods of 3, 4, 5, and 6 wk to separate seed beds. The treatments

¹ Thanks are due to Shri Ranjan for his guidance and helpful criticism and for the facilities provided in the Department of Botany of Allahabad University for carrying out this investigation. I am grateful to C. M. Bastia for his help in the preparation of the diagram.

² Short-day treatment consisted of a daily 10-hr exposure to natural daylight in the open field, from 8:00 A.M. to 6:00 P.M. For the remainder of the 24-hr cycle, i.e., from 6:00 P.M. to 8:00 A.M. of the next day, the pots were removed to a well-ventilated dark room.

Long-day treatment consisted of a 24-hr continuous illumination obtained by supplementing the natural daylight with artificial illumination from a 1000-w gas-filled Osram bulb. The bulb was hung at a height of 5 ft, and the intensity of light falling on the surface of the soil, as measured by a Weston phototronic foot-candle meter, was 30-40 ft-candles. The pots were arranged in concentric circles on the ground and their respective positions were interchanged every day so that each pot received almost the same intensity of light.

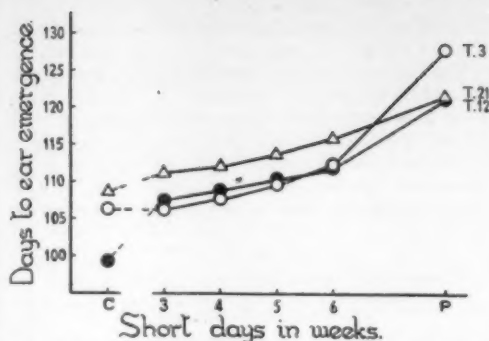


FIG. 1. C, control; P, short-day treatment prolonged until the time of ear emergence.

were arranged so that all were completed on the same day (Aug. 7) and the seedlings were transplanted on that day. After the short-day treatment was over, the seedlings were kept in the pot culture house under environmental conditions identical with those of the control plants which were sown and transplanted on the very same day as the plants from treated seeds. In another set, after 6 wk of short days in the seed bed, the short days were continued till ear emergence was noted in all the plants. Data for ear emergence of the main shoot are graphically represented in Fig. 1. A study of this figure shows that there is a gradual delay in the time of ear emergence as the duration of short-day treatments is increased in the seed bed and thereafter. In the experimental set where the short days were prolonged until heading, the delay was very marked. The photoperiodic behavior of these 3 medium-early varieties is somewhat akin to that of the 4 early varieties T.136, T.N.22, T.N.27, and Ch.10 of U.P. (2). Similar results were obtained by Sircar and Ghosh (3) in Charnock and Panbira, 2 summer varieties of rice of Bengal, by the application of 8-hr short days. Sircar and Parija (4), however, have not obtained any delaying effect in Jhanji 34 and Bhutmari 36, 2 other summer varieties of Bengal, by giving similar treatments. Kar (5), after giving long and short days for only 15 days to 2 summer and 8 winter varieties of rice of Bengal, made a general statement that in different varieties of paddy, high temperature associated with short day lengths was inductive to earliness and that low temperature or longer day lengths produced retardation. In the light of the present investigation, Kar's statement needs modification. In these 3 medium-early varieties of rice of U.P., short days did not induce earliness but rather they greatly prolonged the time of ear emergence. The photoperiodic behavior of medium-early varieties stands quite in contrast to those of late or winter varieties of rice where considerable earliness is obtained by application of the same short-day photoperiod (6). The response to photoperiod in rice is thus greatly varietal and is largely controlled by the agricultural characteristic of the predominant groups. While studying the

effect of long days on these medium-early varieties it was also seen that 24-hr long days for 3-6 wk in the seed bed brought about a delaying effect on ear emergence. On the basis of their flowering behavior as related to length of day, these medium-early varieties may be classified as intermediates, as they flower within a definite range of length of day, producing flowers less readily when the days are either sufficiently shortened on the one hand or sufficiently lengthened on the other (7, 8).

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The Effect of Adenosinetriphosphate on the Cilia of the Pharyngeal Mucosa of the Frog

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At the present time it is generally agreed that adenosinetriphosphate (ATP) participates widely in the chemical to mechanical energy-converting systems of living organisms. Particularly in the case of muscle, the role of this compound has been studied extensively (1, 2). Bacterial flagellar proteins have been observed to contract when treated with ATP, and bacterial motility is increased specifically by this substance (3). Moreover, the rates of cytoplasmic streaming and amoeboid movement rise after injection of ATP solutions into the tail region of *Amoeba discoides* (4). In the present report, data summarized show that the movement of cilia of the pharyngeal mucosa of the frog is strikingly accelerated in the presence of ATP. Thus, the evidence suggests that ciliary activity may be included among the various types of cellular movement related to this ubiquitous compound.

Ciliary activity was measured in terms of the rate of transport of a standard object across the ciliated pharyngeal mucosa of the frog (*Rana pipiens*), using a technique generally similar to the method employed by Stewart (5). In each of 29 experiments, the pharyngeal mucosa of a pithed frog was dissected free of underlying tissues and pinned with slight traction to a weighted cork. The preparation was immersed in 20-200 ml aliquots of specified test solutions in a paraffin-lined or glass container. The time required for the transport of a piece of aluminum foil (weight = 0.1 mg; area ca. 1 mm²) along a 1-cm distance in a hori-

TABLE 1
EFFECT OF ATP (1.5×10^{-4} M) ON THE RATE OF
TRANSPORT OF A TEST OBJECT ACROSS
THE CILIATED MUCOSA

Solution in which tissue was immersed	Number of experiments	Rate of transport mm/10 sec	Rate of transport relative (initial control = 100)
Initial control Ringer's solution (pH = 7.14)	9	4.3 ± 1.4	100
Ringer's with ATP (1.5×10^{-4} M) (pH = 7.18)	9	8.1 ± 1.7	196 ± 40
Final control Ringer's solution (pH = 7.14)	9	3.9 ± 1.4	91 ± 13

zontal plane was measured, and the rate of transport (mm/10 sec) was calculated. The detailed procedure was as follows: 6 rate determinations were made in the control solution (buffered amphibian Ringer's solution). The mucosa was then transferred to an experimental solution containing ATP and 6 determinations were again made. Finally, the ciliated tissue was placed in a fresh aliquot of control Ringer's solution, and the rate was measured as before. A 1-min equilibration period was allowed, after transfer of the tissue to the new immersion medium, before measurements were made. All solutions were at room temperature (ca. 22–26° C). The concentrations of solutes in the amphibian Ringer's solution were 0.124 M for NaCl, 1.1 mM for CaCl_2 , 1.9 mM for KCl, 2.4 mM for NaHCO_3 , 0.7 mM for NaH_2PO_4 , and 1.11 mM for glucose.¹ ATP—in the form of the sodium salt, $\text{Na}_3(\text{ATP}) \cdot 3\text{H}_2\text{O}$ —was present in concentrations of 1.5×10^{-5} M, 1.5×10^{-4} M, or 1.5×10^{-3} M. In some experiments, the effect of ATP hydrolyzed according to the method of Lohmann (6) was tested.

In every instance in which ATP was present in the Ringer's solution, ciliary activity increased markedly. The data summarized in Table 1 show that the rate was approximately doubled in 1.5×10^{-4} M ATP. The effect was reversible, for, when the mucosa was transferred to a fresh lot of control Ringer's solution, the activity was noted to fall to a level close to the control rate (Table 1). The time required for these alterations was brief, since the changes had become fully established by the end of the standard 1-min equilibration time. A maximal response was seen with ATP concentrations as low as 1.5×10^{-5} M, and a 100-fold increase

¹ It may be noted that this solution contained glucose as substrate and Mg^{++} magnesium ions. In further experiments a modified Krebs-Ringer phosphate solution (242 mOsm/l) was used which contained MgSO_4 at a concentration of 1.14 mM and had no substrate. Since the results of these experiments were closely similar to the results discussed above, it was concluded that neither the absence of Mg^{++} nor the presence of glucose was a significant factor in determining the effect of ATP on ciliary activity.

in ATP concentration did not result in an appreciable further increase in rate (Table 2). In specimens in which initial activity in Ringer's solution was irregular, it became stabilized in the presence of ATP. Moreover, in one experiment where no ciliary activity could be detected under control conditions, the addition of ATP was followed immediately by the onset of ciliary movement. Solutions containing a hydrolyzate of ATP were without any effect on the rate of ciliary activity (Table 2).

TABLE 2
EFFECT OF VARIOUS SOLUTIONS ON THE RATE OF
TRANSPORT OF A TEST OBJECT ACROSS
THE CILIATED MUCOSA

Solution tested	Number of experiments	Rate of transport mm/10 sec	Relative rate of transport (initial control = 100)
Control Ringer's solution (pH = 7.14)	27	4.3 ± 1.3	100
Ringer's with ATP 1.5×10^{-5} M	5	9.3 ± 1.1	210 ± 31
Ringer's with ATP 1.5×10^{-4} M (pH = 7.18)	9	8.1 ± 1.7	196 ± 40
Ringer's with ATP 1.5×10^{-3} M	5	10.1 ± 2.5	292 ± 100
Ringer's with hydrolyzate of ATP 1.5×10^{-4} M (pH = 7.12)	4	3.0 ± 0.7	94 ± 11

The accelerating action of ATP on the ciliary movement of the frog's pharyngeal mucosa may be described, in summary, as highly consistent, rapid, reversible, and demonstrable in the presence of relatively low concentrations of ATP. The effect appears to be specific in that hydrolysis of the substance abolishes completely its effect on the test system. The mechanism of action of ATP on ciliary movement is still unclear, however, for the compound may affect the ciliary contractile elements directly or indirectly (through concomitant alterations in the cell membrane). In spite of their obvious significance in general physiology and in medicine, problems of ciliary activity have been somewhat neglected of late. They warrant careful reinvestigation in the light of recent developments in the field of cell physiology and biochemistry.

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Evidence that Molybdenum Is a Nondialyzable Component of Xanthine Oxidase^{1,2}

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Isolation and purification of xanthine oxidase from the milk of cows that have received Mo⁹⁹ has provided evidence that molybdenum is an integral part of the xanthine oxidase of milk and, presumably, of other sources. This finding is in accord with the evidence of Westerfeld and Richert (1) for the existence of a nutritional factor essential for the production and maintenance of rat intestinal xanthine oxidase and the identification of this factor as molybdenum by De Renzo *et al.* (2).

Labeled sodium molybdate was injected intravenously into a dairy cow and xanthine oxidase was isolated by the method of Ball (3) from milk collected one to several days thereafter. This procedure was repeated with the same cow 2 wk later. In all cases after the initial removal of excess molybdenum by one or two treatments with 25-40% ammonium sulfate, the ratio of Mo⁹⁹ to xanthine oxidase activity remained essentially constant despite rigorous purification procedures, as indicated below for a typical sample. Xanthine oxidase was estimated by Kalekar's method (4) and Mo⁹⁹ by radioassay procedures (Table 1).

That the Mo⁹⁹ was not removed from, and probably did not enter, the xanthine oxidase merely by exchange was demonstrated by addition of 2 g of ammonium molybdate to a sample of milk from the treated cow and subsequent isolation of the enzyme. This treatment with inert molybdenum did not change the ratio of Mo⁹⁹ to xanthine oxidase. In another dilution experiment, nonradioactive milk (126 units of xanthine oxidase) was mixed with an equal amount of radioactive milk (46 ct/sec/unit of xanthine oxidase; 10.6 ct/sec/unit of xanthine oxidase after purification; 91 units of xanthine oxidase). After isolation of the enzyme and dialysis against water for 40 hr, the xanthine oxidase had a value of 4.23 ct/sec/unit in good agreement with the value of 4.43 expected if there were no exchange of the excess Mo⁹⁹ with the inert molybdenum of the nonradioactive xanthine oxidase.

Spectrophotometric data suggest a molar ratio of flavin to molybdenum of 2:1.

Molybdenum has been recognized for a long time as an essential nutrient for plants, serving metabolic functions involved in the utilization of nitrogen. It

TABLE 1

	Mo ⁹⁹ Ct/sec/unit xanthine oxidase
Milk	1095
Cream	71
Na ₂ HPO ₄ extract	67
Na ₂ HPO ₄ extract after CaCl ₂ treatment	88
Xanthine oxidase after 1st (NH ₄) ₂ SO ₄ ppt	12.1
Xanthine oxidase after 2nd (NH ₄) ₂ SO ₄ ppt	12.6
Xanthine oxidase after 20-hr dialysis	10.9
Xanthine oxidase after 40-hr dialysis	10.6
Average for 4 different purified samples (7 milkings)	10.61 (range 10.4-10.78)

would now seem that molybdenum also plays an essential role in animals, at least to the extent that xanthine oxidase is concerned with necessary metabolic processes. In addition, the toxic behavior of excess molybdenum in the copper-molybdenum imbalance may possibly be explained in terms of oxidase activity.

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Intracellular Localization of Labeled Nucleic Acid Determined with Autoradiographs¹

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Autoradiographs have been used to detect incorporation of phosphorus (P³²) into the deoxyribose nucleic acids (DNA) of individual nuclei (1, 2). In this way the time of synthesis of DNA in relation to the division cycle during mitosis and meiosis has been determined. The method is also applicable to the study of phosphorus incorporation into the ribonucleic acids (RNA) of single cells. By applying a thin photographic emulsion layer to serial sections of large cells and making autoradiographs as previously described (2), the radioactive element can be located with sufficient precision to determine its intracellular distribution. For example, in the large cells of the gastric caeca and salivary glands of the third instar larvae of *Drosophila*, the relative rates of incorporation of P³² into the RNA of cytoplasm, chromatin, and nucleolus can be followed.

Early third instar larvae of *Drosophila repleta* were

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fed P^{32} in the form of inorganic phosphate (120 $\mu\text{c}/\text{ml}$ of water containing 30 mg of gelatin and 30 mg of brewers' yeast). Incorporation occurs most rapidly in the cells of the salivary glands and the gastric caeca, and the comments here refer to the behavior of these cells. At intervals of 1 hr after beginning to feed on the labeled food, larvae were fixed in Carnoy's fluid, and prepared as paraffin sections (7 μ) on slides.

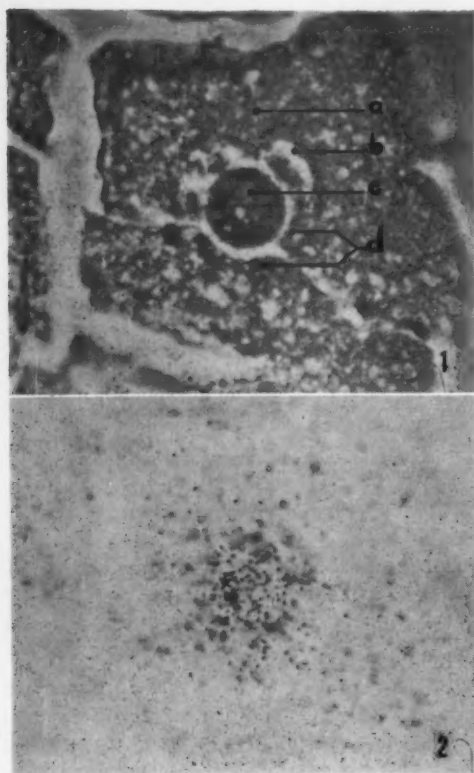


FIG. 1. Autoradiograph of a cell of the gastric caecum fixed 1½ hr after feeding food containing P^{32} . 1. Phase photograph of the cell; the structures indicated are (a) cytoplasm, (b) nuclear membrane, (c) nucleolus, (d) chromatin. 2. Bright field photograph showing distribution of silver grains above the same cell. $\times 1220$.

After passing these slides through hot ether-alcohol, washing in lower grades of alcohol, cold 5% trichloroacetic acid, and water, one of a pair of slides containing tissues of the same larvae was coated with autoradiographic stripping film. The other slide was placed in a solution of protease free ribonuclease² (0.2 mg/ml of water at pH 6.0 for 2 hr at 37°) (3). After this digestion, or in some experiments after hydrolysis and staining by the Feulgen procedure, the second slide of the pair was coated with stripping film.

A study of the autoradiographs, from those larvae

² Prepared by Worthington Biochemical Co.

fixed 1 hr after beginning to feed on the labeled food, shows that the highest concentration of P^{32} that remains after fixation and the subsequent washings is in the nucleolus (Fig. 1). About one-tenth this concentration is present in the cytoplasm. Some cells at this early period also show a relatively high concentration in certain regions of the chromatin. The concentration may exceed that in the nucleolus.

Those larvae fixed 2 or 3 hr after beginning to feed show an increasing concentration of P^{32} in all parts of the cell. In 2 hr the concentration of P^{32} in the nucleolus is higher than in the chromatin and the cytoplasm has one-fifth to one-third the concentration present in the nucleolus. If the larvae are removed to nonradioactive food enriched with yeast after the first 2 hr, the P^{32} is still higher in the nucleolus than the cytoplasm 1 hr later, but in 2-3 hr (4-5 hr after beginning to feed on the radioactive food) the P^{32} is about equally distributed in various parts of the cell. Nearly all the P^{32} that remains in the nucleolus and most of that in the cytoplasm and chromatin is removed from the cells on the slides digested in ribonuclease or subjected to the Feulgen hydrolysis (1N HCl for 10 min at 60°). This is interpreted to indicate that most of the P^{32} is incorporated into ribonucleic acids. The P^{32} remaining after digestion or hydrolysis is usually one-tenth or less of the total and its distribution is rather uniform throughout the cell.

Resolution of structures 2-3 μ apart is theoretically possible (4) with this type of autoradiograph. In practice one has the added advantage that adjacent structures may be separated in serial sections. If a nucleolus with surrounding chromatin and cytoplasm of a cell is included in one section, a part of the chromatin of that cell with surrounding cytoplasm in the succeeding section, and only cytoplasm in a third section, estimation of the isotope in each of these three parts can be made with greater precision than would otherwise be possible. In this way, with thinner sections, one should be able to resolve structures in smaller cells. In the cells of *Drosophila*, which are 40-50 μ in diameter with a nucleus 18-20 μ in diameter and a nucleolus 8-12 μ in diameter, resolution is not a problem.

A large proportion of the nuclear RNA of higher specific activity than cytoplasmic RNA previously reported (5-7) may be contributed by nucleolar RNA. The nucleolus may be a center of RNA synthesis as suggested by Pollister and Leuchtenberger (8) or a reservoir of RNA produced in other parts of the nucleus. The initial high specific activity of chromatin observed in these autoradiographs suggests the latter. Although one cannot definitely answer questions of sites and rates of synthesis yet, the technique provides a tool by which variations in turnover rates may be studied at the intracellular level. Perhaps the role of RNA can eventually be evaluated by application of this technique along with photometric techniques that allow measurement of relative concentration of certain cellular constituents.

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Gastric Ascorbic Acid in the Gastritic Guinea Pig¹

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Among other things, the rat differs from the human in having a squamous forestomach and an endogenous supply of ascorbic acid. When it was found (1) that a chemically induced gastritis in the rat resulted in a decrease of ascorbic acid in the stomach and adrenals, it became of considerable interest to determine if a similar relation exists in an animal having an entirely glandular stomach and lacking endogenous ascorbic acid. The present study, therefore, was carried out on the guinea pig.

TABLE 1

EFFECT OF EUGENOL ADMINISTRATION ON GASTRIC AND ADRENAL ASCORBIC ACID IN THE GUINEA PIG

No. of guinea pigs*	Treatment	Chem. form	Mean ascorbic acid	
			Stomach (mg %)	Adrenal (mg %)
11	H ₂ O controls (st)†	Oxidized	1.5 ± 0.69	5.3 ± 3.0
		Reduced	14.4 ± 0.42	117.7 ± 7.2
		Total	15.9 ± 0.52‡	123.0 ± 7.5
10	Eugenol (st)‡	Oxidized	1.0 ± 0.25	3.4 ± 2.9
		Reduced	7.9 ± 1.8	84.4 ± 4.4
		Total	8.9 ± 1.9	87.8 ± 2.6

* Weight loss not observed in any animal.

† By stomach tube.

‡ Differences between corresponding totals from the two groups are statistically significant. $P < 0.01$.

Male Rockland Farms guinea pigs weighing 350-450 g received Purina Rabbit Chow Checkers³ and tap water ad libitum as well as daily intramuscular injections of 25 mg sodium ascorbate in 1.0 ml physiological saline. The guinea pigs were divided into 2 groups. The first group, controls, received 3-ml oral

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³ Preliminary analysis of our stock of Purina Rabbit Chow Checkers indicated that the concentration of ascorbic acid was < 0.08 mg %.

doses of water daily for 7 days. The second group received the same amount of a 1.0% emulsion of eugenol. The ascorbic acid was determined by the method of Roe *et al.* (2).

Introduction of the eugenol emulsion to the gastric lumen by stomach tube brought about a grossly evident gastritis which was absent in the water-fed controls. The total ascorbic acid concentration in the stomachs of the gastritic guinea pigs was significantly decreased by approximately 44%. In the same animals there was a simultaneous decrease of about 29% in the adrenals, which was probably associated with a systemic stress response. The ratio of oxidized to reduced ascorbic acid in the stomachs and adrenals of the gastritic animals was not significantly different from that in the controls (Table 1). The decrease in gastric tissue ascorbic acid during an induced gastritis is more pronounced in the guinea pig (44%) than in the rat (13%) (1). In the rat a smaller decrease of gastric ascorbic acid resulted, apparently because part of the loss was simultaneously replenished from biosynthetic sources.

The data suggest that the ascorbic acid decrease in the stomach of both species during gastritis is a result of rapid utilization of vitamin C at a site of regeneration. The rapid utilization of ascorbic acid at sites of regeneration also has been suggested by the work of Leise *et al.* (3), who reported that the percentage of takes in transplantation of a C 954 hepatoma is increased from 36 to 52% in C57L(Fx) mice when supplementary ascorbic acid is supplied. Moreover, Minor and Ramirez (4) have reported that cancer patients utilize more ascorbic acid than patients having nonmalignant disease, as determined by daily measurement of ascorbic acid intake and excretion. The present work suggests a similar rapid utilization of ascorbic acid in the gastritic mucosa.

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Chromosomal Interchanges as a Basis for the Delimitation of Species in *Oenothera*¹

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The delimitation of two species upon the basis of their failure to form a hybrid is untenable wherever

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single or few gene differences or simple structural heterozygosity leads to the formation of nonviable combinations. Incipient species may owe their origins to differences such as these, but the accumulation of further differences must follow before what was once a single species may be considered as two. It is probably undesirable that there be any agreement concerning the exact degree of introgression which might be allowed between two taxa which yet remain as separate species. When, however, the differences between the two taxa become appreciably greater than the variation within each of these taxa, the two are certainly approaching the level of species. Conversely, the occurrence of as great or greater variation within two taxa than between them must place the two taxa in subspecific rank under a single species. The latter point of view will be used to show that two long-recognized species of *Oenothera* are probably only variations of a single species.

In a general survey of the cytogenetics of *Oenothera* subgenus *Raimannia*, Hecht (1) pointed out that *Oenothera affinis* Camb. and *Oenothera mollissima* L. might represent extremes in variation of a single species. This possibility has been considerably strengthened following a more detailed study involving six races of each of these two species (2). Morphologically *O. affinis* is distinguished from *O. mollissima* by its longer hypanthia and longer petals; cytologically, it was found that all the races of *O. mollissima* are complex heterozygotes with a circle of 14 chromosomes, whereas *O. affinis* includes complete homozygotes, intermediate types, and complex heterozygotes like those of *mollissima*.

Specific relationships in *Oenothera* are complicated by the fact that circle-of-14 types are a special type of species, consisting of two distantly related genomes maintained in a condition of permanent heterozygosity by virtue of a system of balanced lethals which prevents the formation or survival of the homozygous combinations. However, when two circle-of-14 races are crossed, the progeny may show pairing of at least some of their chromosomes. The number of pairs thus obtained is a measure of the relatively recent common origin of the chromosomes of the two genomes combined in the new hybrid, and therefore is a measure of the relationship of the parental genomes.

Six geographical races each of *O. affinis* and *O. mollissima* were crossed with each other in all possible combinations. Mature progeny were obtained from 28 (30 possible) of each of the intraspecific crosses and from 63 (72 possible) of the interspecific crosses. Many of these hybrids included two to four classes of progeny which differed in chromosome configuration, and may therefore be considered as different combinations of genomes. Combinations that indicated a difference of no more than 3 interchanges were considered to indicate a relatively close relationship, whereas 4 to 6 interchanges were considered as indicative of a more remote common origin of the genomes involved. Of the 50 interracial *affinis* combinations 39 (78%) differed by 3 or less than 3 interchanges. Only 4 of the

43 interracial *mollissima* combinations (10%) differed by 3 or fewer interchanges. Thirty-one per cent (34 out of a total of 108) of the interspecific combinations were similarly found to have closely related genomes. It appears, thus, that the genomes of *affinis* are more closely related to those of *mollissima* than are the *mollissima* complexes to each other. *O. affinis* and *O. mollissima* have essentially contiguous distributions in southern South America (3), and the evidence above strongly suggests that introgression occurs. Under these circumstances it is probable that *O. affinis* Camb. (and its several synonyms) should be included under the prior epithet *O. mollissima* L.

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Protein Metabolism and Interactions¹

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This note applies and extends the methods of Sprinson and Rittenberg for the interpretation of protein metabolism and interactions (1). There is now available a sufficient quantity of experimental results (from widely scattered sources) to form the basis of an outline of body protein reactions.

The main or overall protein reactions may be interpreted on the basis of the simplified scheme of Fig. 1. The k 's represent rate constants, and all the reaction rates are assumed to be first order with respect to the reactant.

Let A be the total amount of body protein and let f_j ($j=1, 2, 3$, or 4) be the fraction of that which is in protein x_j . Then if x_{j0} is the amount of protein x_j when a balanced steady state is maintained, it follows that $x_{j0} = f_j A$. In this formulation k_{j0} is the turnover rate of protein x_j , and the fraction $k_{j0}/(k_{01} + k_{02} + \dots + k_{0n})$ may be called the fraction of exogenous protein. This fraction, $k_{j0}/(k_{01} + \dots + k_{0n})$, is given by the A of Sprinson and Rittenberg's Eq. (1) (1). They found that this fraction is about 0.5 in normal adults on diets of their own choice. They also found that the corresponding substance, y , has a half-time of only about one-half day in the body. The results of Maas *et al.* (2) on the injection of rats with radioactive

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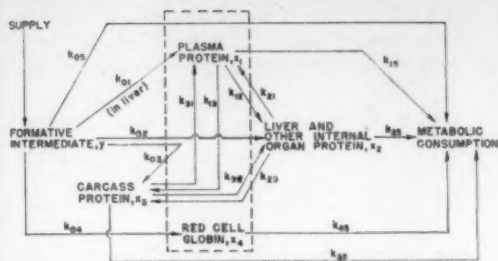


FIG. 1. Simplified scheme of the main or overall protein reactions. The dotted box encloses portions of the scheme involving blood components or transportation by blood.

sulfur show tagging peaks of short duration in the liver and kidney. These peaks probably represent some of the exogenous fraction of y . The individuals on the minimum essential diets of Rose (3) were probably getting negligible quantities of protein that would enter this exogenous fraction of y . In other words, k_{05} was then approximately zero.

When N^{15} -tagged amino acid is fed over a period of a few days, most of the body protein tagging is that of x_1, x_2, x_3 , and x_4 , which may be called endogenous protein (4, 5). Let

$$T_j = 1/k_{js} \quad (1)$$

be called the average utilization time of protein x_j . This is observed by the isotopic tagging of one constituent element, such as nitrogen, so it refers to the utilization of that element in the protein x_j ($j=1, 2, 3$, or 4). Let

$$H_j = (\text{a constant}) \cdot k_{0j}/f_j \quad (2)$$

be the greatest initial tagging, or curve height, for protein x_j (often in units of atom per cent excess). The constant in Eq. (2) is independent of j and is a true constant for any individual in a balanced steady state. To maintain such balance

$$f_1 k_{1s}/k_{01} = f_2 k_{2s}/k_{02} = f_3 k_{3s}/k_{03} = f_4 k_{4s}/k_{04} \quad (3)$$

From Eqs. (1), (2), and (3)

$$H_1 T_1 = H_2 T_2 = H_3 T_3 = H_4 T_4 \quad (4)$$

As far as globin is concerned, the above equations are equivalent representations that accurately portray only the average values. In actuality, globin is incorporated in red cells by the bone marrow, these are gradually released to the circulating blood, and the globin is essentially inert until its red cells break down several months later. The experimental studies of tagged globin (6, 7) may be interpreted as showing that T_4 is about 130 days (8). Sprinson has stated (9) that in the experiment of our reference (7) the observed H_1/H_4 was about 4.6, so from Eq. (4) T_1 is about 28 days.

Also let T_s be the average overall utilization time for the whole body so that

$$f_1/T_1 + f_2/T_2 + f_3/T_3 + f_4/T_4 = 1/T_s \quad (5)$$

Since the average 40-kg man has a little over 4 kg of protein, Rose's findings (3) imply that T_s is about 100

days. The experiments of Shemin and Rittenberg on rats (4) show that $H_2/H_3 = T_3/T_2$ is about 5. These values, together with reasonable estimates of the f_j 's, convert Eq. (5) to

$$0.05/28 + 0.18/T_2 + 0.65/5T_2 + 0.12/130 = 1/100$$

Thus T_2 is about 42 days and $T_3 = 5T_2$ is about 210 days. A summary of these overall average values is:

Protein	x_1	x_2	x_3	x_4	Total
Fraction of total, f_j	0.05	0.18	0.65	0.12	1.00
Av. util. time, T_j (days)	28	42	210	130	100
$k_{js} = 1/T_j$	0.036	0.024	0.0048	0.0076	0.010

This formulation implies that the average isotopic excess of the whole body decreases daily about 1/100th of its value throughout the course of tagging experiments.

All body proteins except globin appear also to be involved in active interactions, because all their isotope curves eventually approach a level of slow decline at or near that of the average isotope concentration. According to the scheme suggested here, these interaction reactions would satisfy the differential system.

$$\frac{dx_1}{dt} = k_{21}x_2 + k_{31}x_3 - (k_{12} + k_{13} + k_{1s})x_1$$

$$\frac{dx_2}{dt} = k_{12}x_1 + k_{32}x_3 - (k_{21} + k_{23} + k_{2s})x_2 \quad (6)$$

$$\frac{dx_3}{dt} = k_{13}x_1 + k_{23}x_2 - (k_{31} + k_{32} + k_{3s})x_3$$

$x_j = x_j(t)$ = amount of isotopic excess in protein x_j at time t (const. $\times f_j \times$ at % excess), and

$$x_j(0) = H_j \quad (j=1, 2, \text{ or } 3)$$

The solution of this system has the form

$$x_j = C_{j1} \exp(-r_1 t) + C_{j2} \exp(-r_2 t) + C_{j3} \exp(-r_3 t) \quad (7)$$

($j=1, 2, \text{ or } 3$)

where the C 's are determinable functions of the H 's and the $-r$'s are roots of the determinantal equation

$$\begin{vmatrix} (r + k_{12} + k_{13} + k_{1s}) & -k_{21} & -k_{31} \\ -k_{12} & (r + k_{21} + k_{23} + k_{2s}) & -k_{32} \\ -k_{13} & -k_{23} & (r + k_{31} + k_{32} + k_{3s}) \end{vmatrix} = 0$$

It has been shown (10) that $x_1(t)$ is of the form of Eq. (7). The experimental results that would be needed for the estimation of all the k 's are neither available nor readily obtainable at this time. However, the derivatives of Eq. (6) can be approximated by the quotient of finite differences, $\Delta x_j/\Delta t$ ($j=1, 2$ or 3), and one can then see from the data of Shemin and Rittenberg (4) that at least some of the interaction k 's are of the same order of magnitude as the overall turnover k 's (k_{js} , or $1/T_j$).

Some of the interactions probably also involve one or more intermediates that can be transported by the blood. For example, this is likely to be the case in the carcass-internal organ protein interaction.

More detailed results can be obtained for the plasma proteins by using London's curves of N^{15} -tagged plasma (5), together with Dole's values for the com-

position of normal plasma (11). The isotopic excess in each plasma component was found to decline exponentially toward the average isotope concentration. In particular, the fractions of the plasma component isotopic excesses which interact daily are estimated at about 0.05, 0.5, 0.09, 0.06, and 0.09 for albumin, α -globulin, β -globulin, γ -globulin, and total plasma protein, respectively. Of the 0.09 value for total plasma protein only $1/T_1$, or about 0.036, could be attributed to plasma protein replacement from newly consumed protein.

On injecting dogs with tagged plasma protein, Yuile, Lamson, Miller, and Whipple obtained evidence of similar quick uptakes and subsequent interactions (12).

Also, the results estimated here for the various plasma components serve to illustrate the fact that all the other estimates are only averages of quantities having widely varying components.

Probably all the proteins that undergo the described

interactions, as well as the relatively small amounts of nonprotein nitrogen, are the main constituents of the so-called nitrogen pool of the body.

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Comments and Communications

The Phospho-Di-Anhydride Formula and Its Relation to the General Structure of the Nucleic Acids

SINCE the publication of the author's originally proposed phospho-tri-anhydride structure for the nucleic acids (1), Markham and Smith (2) have reported that both mono- and di-nucleotides possessing cyclic anhydride linkages and phospho-di-ester dinucleotides were products of the enzymatic degradation of yeast ribonucleic acid. Further, Cohn and Volkin (3) have succeeded in demonstrating the presence of 5-phospho-nucleotides in the digest of calf liver ribonucleic acid, which in itself is not incompatible with the phospho-tri-anhydride structure. More recently, Merrifield and Woolley (4) have presented conclusive evidence for the presence in yeast ribonucleic acid of "dinucleotides having two phospho-sugar ester bonds on one nucleoside and dinucleoside phosphates which have two nucleosides attached to one phosphate." These authors, aware only of the tri-anhydride structure, have concluded that their results "... do not seem to conform to the structure recently proposed by Ronwin." This conclusion is justified only when consideration is narrowed to the special case of the phospho-tri-anhydride structure (1); however, the results of these authors, together with those of the others mentioned above, are quite compatible with the amplified form of the P-O anhydride polymer core formula that is being presented here.

In addition, the author has recently become aware of the earlier synthesis of compounds possessing five oxygen atoms bound to a single phosphorus atom (5),

which provides a precedent for the anhydride types that are proposed. The amplification is assisted diagrammatically by Fig. 1.

Section A is essentially one-half a unit cell for a phospho-di-anhydride structure for the nucleic acids along the same pattern as the previously proposed phospho-tri-anhydride structure (1). It is to be noted that all the nucleosides are depicted as engaged in diphospho-ester linkages that can give rise to such products as described by Merrifield and Woolley (4) and Markham and Smith (2). Each phosphorus atom carries one primary dissociation. Were the bond, P_2-O-P_3 of Sec. A, Fig. 1 hydrated, there would result two secondary dissociations in addition to the four primary dissociations already shown. This condition would split the P to O polymer core, but the chain would still be intact. Though the bases are pictured as parallel, but not coplanar to the sugar moieties (only the nuclei are shown), in accordance with Astbury's description (6, 7), they may be and probably are perpendicular to the D-ribose rings as recently reported for cytidine by Furberg (8, 9).

All the half-cells of any nucleic acid (either the ribo- or deoxyribo types) may possess the structure shown in Sec. A, Fig. 1 (the phospho-di-anhydride type) or they may all conform to the originally proposed phospho-tri-anhydride formula (Sec. B, Fig. 1) in which all the nucleosides are mono-esterified. As another condition, they may all assume the phospho-di-anhydride core wherein the nucleosides are bound as cyclic anhydrides (2) as depicted in Sec. C, Fig. 1. In this case, there is illustrated a situation in which three primary and one secondary dissociations are present for four P atoms. Another type of di-anhy-

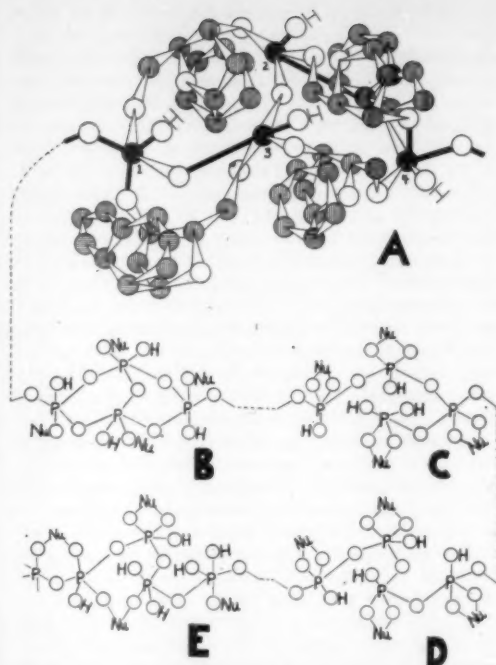


FIG. 1. The phospho-di-anhydride formula and variations of nucleic acid structure. Section A: closed circles, phosphorus atoms; open circles, oxygen atoms; vertical-lined circles, carbon atoms; and horizontal-lined circles, nitrogen atoms. Bond distances, bond angles, and relative atom and group sizes are not depicted exactly. The hydrogen atoms and other groups that are present on the bases and sugar moieties but which do not partake in the proposed bonding types have been omitted to avoid unnecessary confusion of the diagram.

Sections B, C, D, and E: the symbol Nu represents a nucleoside that is always shown in these diagrams as bound to the phosphorus atoms in phospho-ester linkages. Other atoms are conventionally designated.

drude structure having four primary dissociations for four P atoms and all nucleosides bound in cyclic anhydride linkages is pictured in Sec. D, Fig. 1. Then again, each unit half-cell may have a sprinkling of all types of linkages as diagrammed in Sec. E, Fig. 1. In this section there is also illustrated the linking of a nucleoside in a diphospho-ester grouping that involves P atoms from adjacent unit half-cells. As another possibility for structural variation, a nucleic acid may have a combination of any and all of the unit half-cell types (Sec. A-E, Fig. 1) and others which are necessarily not shown.

Thus it is proposed that the structure of any nucleic acid is described by either the full phospho-di-anhydride or the full phospho-tri-anhydride formulas or as lying somewhere between these two extremes.

Considerations concerning end group types, branching, the unit cell structure and dimensions, titration data, the sequence of nucleosides, and the stability of nucleic acids that were previously applied to the phos-

pho-tri-anhydride formula (1) are equally applicable.

The writer is indebted to C. Neuberg, Department of Chemistry, Polytechnic Institute of Brooklyn, for bringing to his attention the work of Anschutz (5).

The writer also wishes to thank the anonymous referee who pointed out that the purine to pentose link in part A of the figure is erroneously shown at position 3 as is the case for pentose-pyrimidine. He has always been aware of the work of the Gulland and Todd groups which established the point of linkage as position 9, but made an error in drawing the figure. The reader is urged to make a "mental" correction (rotate the purine portion approximately 180° in the same plane and bind at position 9), since the error in the diagram does not affect the basic backbone linkages that are proposed.

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Received June 8, 1953.

A, Comment on the Discussion of Genetics by His Holiness, Pius XII

SCIENCE, even theoretical science, has ceased to be the concern of a small number of devotees secluded in ivory towers. The ideological significance and the consequent importance in human affairs of certain branches of basic science have become widely recognized. The most telling recognition comes from leaders of human thought and action who are not themselves scientists but who feel called upon to concern themselves with problems of theoretical science and to state publicly their attitudes toward these problems. Genetics has been honored by such recognition more than any other biological discipline. It does not matter whether it was Stalin himself or some other communist dignitaries who decided that genetics is an evil product of bourgeois mentality, and that it must be replaced by Lysenko's version of old wives' tales. In either case, these busy men have paid genetics a wholly unintended compliment by expending considerable time and energy to delve into genetical problems.

A vastly greater honor is bestowed upon genetics by the statement of His Holiness, Pius XII, made on September 8, 1953, at the papal summer residence of Castel Gandolfo.¹ Geneticists will be pleased to have

¹ The text of the statement has been published, in original French, in *L'Osservatore Romano*, Sept. 9, 1953.

so high an authority recognize that "among diverse branches of biology, perhaps the most dynamic studies are those of genetics." It is even more gratifying that the aims of genetics "... attract an intense interest of institutions which occupy themselves with man as a moral personality, with his formation, and with his education which should fashion in him a mature and firm character, conscious of his responsibilities, of his method of thinking and of acting in matters that are decisive for the present as well as for eternity." And, indeed, "... philosophy can no longer disregard genetics if it wants to remain in contact with reality in its analysis of psychic activities."

The statement is carefully phrased and is hedged with the reservation that "this is what We should like to borrow from your branch [of science] without wishing to state Our own opinion." It opens with a succinct summary of the basic facts and concepts of genetics, which are said to be well-established positive attainments of science. The cell theory, fertilization, Mendel's laws, the gene theory, and mutation are thus passed in review. It is recognized that acquired traits and mutilations are not inherited, despite the contrary opinion of "Russian geneticists." The relationships between the genotype and the environment are rightly conceived to be dynamic ones, the genotype determining not rigid traits of the organism but rather its norm of reaction to the environment.

It comes, then, as a surprise that a much less hospitable view is taken of evolution. Evolution is certainly not denied, but it is admitted only as a possibility, as a hypothesis not yet verified, the opinion of some scientists which is not shared by others. One is left to wonder who are the "reputable scientists" who are said to have formulated "other hypotheses," and what these hypotheses are. Nor can one agree that the processes whereby one species may give rise to another still remain completely impenetrable. In all modesty and humility, and fully conscious of the admonition that one should not mistake hypotheses and opinions for established facts, a biologist may claim that he has at least some plausible models of how the origin of species may take place.

Moreover, it is factually incorrect to say that "one has not yet succeeded in making a species from another species." The scientific advisers of His Holiness have been guilty of negligence when they have failed to point out that the feat of obtaining a new species in experiment was accomplished more than a quarter of a century ago. The classical example is a completely new plant, *Raphanobrassica*, obtained through allopolyploidy. *Raphanobrassica* is a new species by any reasonable definition, since it is not only distinct in appearance but also reproductively isolated from its ancestors, and yet quite fertile with itself. In recent decades a fair number of new allopolyploid species have been brought into being, and what is more, some allopolyploid species existing in nature have been re-created in experiments.

It is, indeed, incontestable that we do not know the complete story of evolution and do not yet understand

all the mechanisms which bring it about. Most biologists will be willing to go even farther and admit that, despite the great forward strides made in recent decades, the understanding of evolution is still in its infancy. The situation of evolution is, however, not appreciably different from that of other aspects of genetics. Assuredly there is much to be learned also about the mechanisms of the transmission of heredity.

To contrast our knowledge about the transmission of heredity as factual and well established with the knowledge about the occurrence of evolution as hypothetical and conjectural is not in accord with the present status of biological science. No less a geneticist than Goldschmidt still doubts that genes exist and proposes alternative hypotheses concerning this matter. Although Goldschmidt's skepticism is shared by very few of his colleagues, it will be recognized by many geneticists that the theory of the gene is going through a crisis. There is similar diversity of opinion concerning evolution, as is to be expected within a dynamic science during a period of rapid development. The course which the evolutionary process has taken in different groups of organisms (phylogeny), as well as the mechanisms which bring evolution about, are under investigation. But there can be no reasonable doubt of evolution as a historical fact, in the sense that evolution has taken place. This certainty includes the origin of man from nonhuman and pre-human ancestors, although the exact sequence of ancestral and collateral forms is far from adequately known, and the causation of the evolutionary events only dimly discerned. The occurrence of evolution in the history of the earth is well established as can be any event or process not witnessed by human observers, not witnessed for the simple reason that such observers did not yet exist or did not know how to record their testimony.

It is, of course, a fact that anti-evolutionists still exist, and that some Protestant religious denominations seem to be committed to fundamental views. Nor is it to be denied that, while a majority of anti-evolutionists are simply ignorant of the evidence which has led science to accept the evolutionary view of nature, a small minority hold anti-evolutionist opinions despite their being familiar with all the pertinent data. However, the existence of such informed anti-evolutionists is not a biological but rather a psychological problem. Informed anti-evolutionism is a phenomenon much like anti-geneticism of the Lysenko variety. In both cases the opposition arises from powerful emotional biases which make factual evidence and rational argument unable to change preconceived notions. The pronouncement made at Castel Gandolfo does not in any sense belong in this category, for it does not hold evolution to be contrary to or incompatible with Divine Revelation. But, regrettably, it does not show evidence of being well advised concerning the actual state of knowledge in biological science. Taking an over-conservative view in the matter of evolution makes the highest religious authority appear to oppose rather than encourage scientific progress. This is injurious

both to science and to religion, keeping up several centuries of misunderstanding.

The concluding portion of the statement of Castel Gandolfo is concerned with practical applications of genetics. Having been addressed to the participants in the so-called "First Symposium on Medical Genetics," it naturally takes up the problem of defective heredity and its control. Geneticists will be gratified by the recognition that "the fundamental tendency of genetics and eugenics is to influence the transmission of hereditary factors in order to promote what is good and to eliminate what is harmful; this fundamental tendency is irreproachable from the moral point of view." Concerning the methods of accomplishing these ends, genetic counselling is endorsed. The carriers of bad heredity must be warned of the burdens which they are likely to impose upon themselves and their descendants. Eugenic sterilization is nevertheless opposed as a manifestation of "racism," which is explicitly rejected. However, when a carrier of a hereditary defect is incapable of conducting himself as a human being, one is justified in preventing him "in licit manner" from procreating new life. The statement closes with a reiteration that "the practical ends pursued by genetics are noble and worthy of being recognized and encouraged."

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A Jugular Technique for the Repeated Bleeding of Small Animals¹

INVESTIGATORS in various fields have long been plagued by the problem of obtaining repeated blood samples from small laboratory animals. Mice, in particular, have presented just such a problem. To obtain

¹ This technique was developed during the course of investigations supported by the Damon Runyon Memorial Fund for Cancer Research (grant No. 222).

repeated blood samples from the same mouse, a technique for bleeding from the external jugular vein has been developed and used in this laboratory. With the hope that such a technique may be of value to other investigators, an outline of the procedure follows.

Consistent success is dependent upon the animal being in the proper position for venipuncture. The animal is held by grasping the loose skin of the back firmly between the thumb and index finger of the left hand, and the ventral surface of the animal held upwards to expose the neck and upper thorax. Several threads of a 2 × 2 gauze sponge may then be caught on to the upper central incisors of the animal by pulling the taut edge of the sponge forward over the animal's mouth. This sponge is used to hold the head in hyperextension. When working alone, this position may be maintained by pulling the 2 × 2 gauze across the back of the hand and locking it between two fingers (Fig. 1a). In this hyperextended position, depilation from chin to mid-thorax is accomplished with little difficulty and exposes both external jugulars. These vessels are often distended and may be located without difficulty (Fig. 1b).

The puncture approach is determined, dependent upon the distention of the vessels, their size, etc. The needle (26 gage) and syringe should be wet with an anticoagulant. Immature animals, in which the jugulars are small, may be bled by introducing the needle 1- to 2-mm lateral to the sternoclavicular junction. At this point the expansion of the vessel, just cephalad to where it dips under the clavicle, may be visible as a blue, pulsating area. Fewer hematomas were formed when the needle was introduced over the sternum, puncturing the skin 1 to 2 mm below the sternoclavicular junction, and the vessel approached in a caudocephalic direction (Fig. 1c). The blood is withdrawn slowly so as not to cause collapse of these small vessels.

Using this technique, it has been possible to obtain blood samples from weanling mice. Several older animals have been bled a total of twelve times within a

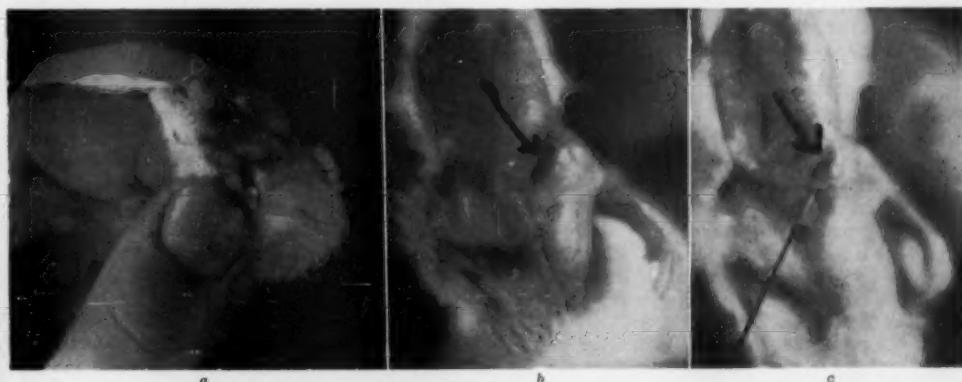


FIG. 1. (a) Mouse held in hyperextension to expose and dilate external jugular veins. (b) Dilated external jugular vein (see arrow). (c) Introduction of 26 gage needle into dilated external jugular vein (see arrow).

period of about six weeks. The method should be readily adaptable to experiments requiring that multiple micro quantities of blood be obtained within a short period of time.

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Sperm Survival in Rodents?

IN SCIENCE, 117, 159 (1953), there is a report by Florence L. Evans of "Unusual Reproductive Phenomena in Rodents." In this report Dr. Evans cites three authentic cases in which a female rat or mouse

dropped a 2nd litter 25-28 days after the first (no mating having occurred in this interval). She suggests that these phenomena involve "delayed implantation of the blastocyst stage," superfetation, or both. Another explanation much simpler than those suggested by Dr. Evans would be to suppose that sperms survived from matings toward the end of the initial pregnancy, and that these sperms were able to fertilize ova which were matured at parturition. It is fairly common to observe rodents in heat at this time. Sperm survival in rodents has also been observed in the vaginal plug for prolonged periods of time.

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Book Reviews

The Human Senses. Frank A. Geldard. New York: Wiley; London: Chapman & Hall, 1953. 365 pp. Illus. \$5.00.

This timely monograph presents a comprehensive description of all human sensations, resting upon a review of 330 papers, with more than a hundred well-chosen illustrations. The contributions of anatomy, physiology, and psychology are skillfully integrated to give a text which is remarkably clear and forceful, written in a distinguished scientific style. The author is fully at home in all three fields and indicates relationships which are brought together in no other single source. The careful descriptions combine the most accurate experimental studies with examples taken from everyday human experience, so that the discussion often becomes an intimate account of the reader's own sensory life, answering many questions never before resolved.

Much of the author's own research has been concerned with the physiology and psychology of vision. His discussions of visual phenomena (4 chs.) are particularly clear, reaching their highest level in an excellent chapter on color vision and color blindness. Only on the anatomical side does the text seem to be somewhat inadequate, resting its argument on older histological descriptions of retinal structure which are surely too simple to explain such phenomena as those of color contrast and spatial interaction. Hartline's recent important work on spatial inhibitions in the eye of *Limulus* (*Symposia on Quantitative Biology*, 17, 125, [1952]) is barely mentioned, and the descriptions of recently discovered collateral connections between visual units in this material were apparently not available in time to influence the text.

The treatment of the phenomena of hearing is lucid (3 chs.), ending in a good review and critique of auditory theories. It is concluded that the original form of the Helmholtz theory is no longer tenable. "A kind of

resonance occurs. The relative amplitudes of vibration of different parts of the basilar membrane . . . change in a regular manner as stimulus frequency is changed . . . but a large portion of the membrane is in operation for all frequencies. The membrane . . . is not a series of stretched transverse fibers. . . [It] is not even under tension."

Three chapters are devoted to the various cutaneous sensibilities. The chapter on pressure and pain, including vibratory sensibility, contains important but little-known material including the author's own studies. The history of the "protopathic-epicritic" theory of Head and Rivers is reviewed, with the author joining the numerous group of students in this field who discount or reject it. The chapter on temperature sensitivity is largely written in terms of the older literature of experimental psychology. New interpretations in this field have become necessary as the result of the very recent physiological work of Zotterman and his colleagues (*Ann. Rev. Physiol.*, 15, 357, [1953]), who have succeeded in recording the nerve impulse discharges along single warm and cold fibers in the tongue of cat and dog.

The treatment of kinesthetic sensibility is rather brief, considering its importance in physiology. The emphasis is properly made that "muscle sense" is largely a matter of joint sensibility, a view which has recently been again confirmed by Mountcastle and his associates (*A.R.N.M.D.*, 30, 339, [1952]). Our newer knowledge of the role of the "small-nerve" efferent fibers in controlling the nervous discharges from muscle proprioceptors has not been covered (Kuffler *et al.*, *A.R.N.M.D.*, 30, 24, [1952]).

In sensory physiology the terms "lumen" and "decibel" are well understood. Less well known is the more recently introduced "dol" scale of pain intensity. Scarcely known at all are the "olfactive" scale for smell and the "gust" scale for taste, resting upon psy-

chological rather than physical determinations. Excellent discussions of these various units are given.

The book transcends the chapters in textbooks of physiology which describe sensory phenomena. It is at once more authoritative than they and more cautious. It avoids the dogmatism so prevalent in the texts, warning against the uncritical tendency to accept early hypotheses and tentative theories as established facts. It repeatedly indicates the direction which research should follow to achieve fuller truth. Even the most serious passages may include a flash of wit or some apt allusion to human experience which helps carry the reader through to the end of the argument.

This volume is probably too serious and too scientific a study to attract the general public, although it could be read with profit by any educated layman. It should be read by every graduate student in the biological and medical fields. Teachers in physiology and psychology will discover here a mine of information from which to draw material for lectures. Research workers will find in it a stimulus to further theory and experimentation.

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Starch: Its Sources, Production and Uses. Charles Andrew Brautlecht. New York: Reinhold, 1953. 408 pp. Illus. \$10.00.

Numerous inaccuracies detract seriously from what otherwise might have been a very useful book on the starch industry. Twelve inaccuracies were counted on the first three pages of Chapter I and eight were counted on the first page of Chapter II. Three examples of errors are: on page one "Monosaccharides are simple sugars with six carbon atoms . . .," is an inaccurate definition as are the definitions of di- and trisaccharides; on page 189 it is stated that "16 to 20 per cent" sulfuric acid is used in corn steeping; on page 207 the figure identified as "Waxy maize factory" is a portion of the sorghum mill at Corpus Christi. Chapter XXI by O. A. Moe contains inaccuracies in structural formulas either from omission of hydrogen atoms or from a stereo-arrangement of carbon atoms. The nomenclature is not that commonly employed today. On page 358, the list of important polysaccharides includes mannans and glucomannans of doubtful importance and omits many generally considered important. The structural formula for guar was not properly accredited to the first publisher of structural data.

The portion of the book dealing with the potato starch industry, a total of 163 pages, is very well written and valuable. Here one will find extensive information on the history and development of the potato starch industry, the agricultural production of potatoes, their grading, handling, composition, and analysis. An excellent and authoritative chapter deals with the manufacture of potato starch. Two of the chapters deal with the sweet potato industry. In the

reviewer's opinion this section on the potato industry is valuable and is recommended to those persons interested in this area.

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Psychiatric Dictionary. With encyclopedic treatment of modern terms. 2nd ed. Leland E. Hinsie and Jacob Shatzky. New York: Oxford Univ. Press, 1953. 781 pp. \$15.00.

Psychiatry, perhaps more than any other medical specialty, has developed a highly complicated technical language of its own. New words are constantly added, definitions are vague and at times strictly personal, and a term may be used with different meaning at different times, thus compounding the confusion. An accurate, authoritative, up-to-date psychiatric dictionary is a great need. The first edition of this dictionary came close to filling this need. Unfortunately, the second edition, if such it can be called, falls far short of such attainment.

Actually, this new edition is a reprint of the first edition as Part I, with a supplement of new words as Part II. In this arrangement lies the work's fatal weakness. From the standpoint of convenience alone, the format is poor. The supplement is approximately half the size of Part I. In effect, this means that one must consult two dictionaries on each word being searched. Economically, many purchasers would have saved money by simply purchasing the supplement separately, since there is no revision of Part I.

These discrepancies, however, are of minor importance compared with the basic fault arising from this method of revision. The primary part of the dictionary is reprinted exactly as in the first edition (1940). This means that many of the changes of the past 13 years have not been incorporated in this "new" edition. Ordinary dictionaries remain relatively static; this cannot be so of a dictionary which covers the lexicon of a science changing as rapidly as psychiatry. The 13-year period overlooked by the authors included a three-year period of partial military mobilization as well as a world war, the latter event being renowned for, among other things, the manner in which it altered psychiatric concepts. Of even more significance, from a lexicographer's point of view, there has been a sweeping revision of the official nomenclature of psychiatric disorders, a revision which has the official support of the American Psychiatric Association, and which has become the psychiatric nomenclature of the American Medical Association's Standard Nomenclature. This item, of no mean significance, has been completely overlooked by the authors.

These oversights seriously impair the usefulness of the dictionary, rendering it not only incomplete, but actually inaccurate. When one seeks a definition of "combat exhaustion," "combat fatigue," or similar terms, one finds them listed in Part II without definition, and with a simple referral to the term "shell-shock" in Part I. In Part I there is given an explana-

tion of "shell-shock" taken from a 1936 publication. Thus evaporates the collected clinical experience of literally thousands of psychiatrists, including some of the most prominent in the field, over seven years of mobilization and combat; the searcher, seeking the definition of a term used perhaps more commonly than any other in the past 10 years, is presented with an explanation written 17 years ago, based on the clinical experience of World War I. This is typical of the omissions throughout the revision.

The revised psychiatric nomenclature was published in early 1952, and has now found its way into at least one standard textbook of psychiatry. Nonetheless, this dictionary, published in 1953, contains not a single one of the new terms. "Acute Brain Syndrome" and "Chronic Brain Syndrome" are nowhere to be found; posttraumatic personality disorder is said to be a "psychosis" as listed in the 1935 nomenclature; and so on. This leads the authors into a ludicrous position from time to time, as when, commenting on the term, "sociopath," they state, "The term has not achieved any considerable degree of acceptance." To the con-

trary, we find the term, "sociopathic personality disturbance" one of the class headings in the Standard Nomenclature. Such inaccuracies are manifold.

Despite these gross defects, the dictionary does have an area of usefulness, provided its limitations are recognized. The authors apparently have devoted themselves assiduously to the literature of psychoanalysis, perhaps to the neglect of the other areas of psychiatry. As a result, the work provides an up-to-date, accurate compilation of psychoanalytic terms, and might very well have been titled "Psychoanalytic Dictionary." In other areas which have been relatively unchanging since 1940, such as the field of psychobiology, the dictionary does a creditable job.

In summary, it may be said that this is an excellent dictionary of psychoanalysis and its allied movements, a good dictionary of psychobiology, and an extraordinarily unreliable reference work in general and clinical psychiatry.

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Scientific Book Register

Adventures in Physiology: A Selection of Scientific Papers. With excursions into autopharmacology. Henry Hallett Dale. London: Pergamon Press. (U.S. distrib.: Macmillan, New York.) 652 pp. Illus. \$19.50.

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- Intergovernmental Cooperation in Highway Affairs*. Special Report 9. iv + 7 pp. Washington 25, D. C.: National Academy of Sciences, National Research Council, 1953. 30¢.
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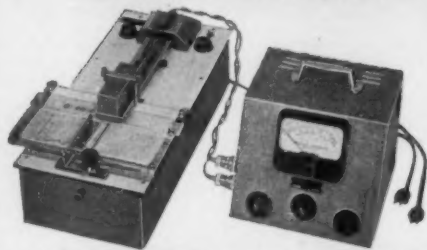
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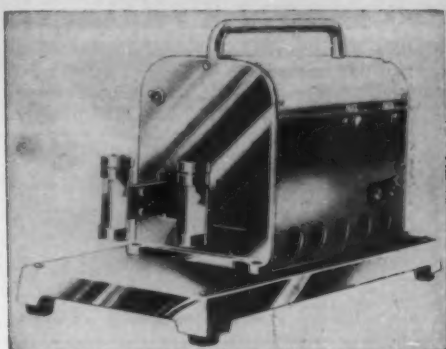


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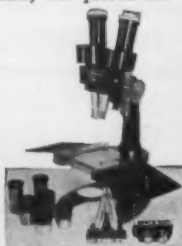
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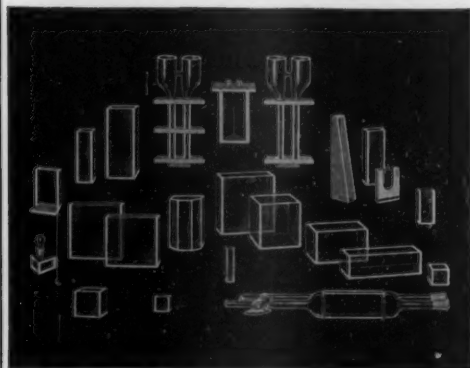
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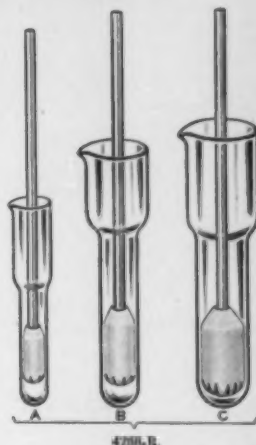
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With Teflon pestle which minimizes powdered glass contamination of the homogenate and reduces heat formation.

Grinding vessel is of Pyrex brand glass precision bore tubing with 2 mm walls.

Grinding space is held to a close tolerance and remains practically constant in extended use.

All components can be autoclaved.



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Teflon has a smooth, waxy surface, is resilient, practically inert, and not wetted by water. Minimizes both heat generated in use and powdered glass in the homogenate, assuring maximal preservation of the accurate relation between pestle and grinding vessel over extended use, and providing

reproducibility of cell lysis essential for quantitative comparison of homogenates from successive samples. See H. Brendler, *Science*, July 20, 1951, p. 61.

Grinding vessel is made of precision bore Pyrex brand glass tubing with walls 2 mm thick and with expanded upper portion for overflow. Clearance between chamber and pestle is held to approximately 0.13 mm. Pestle is furnished with removable rod of either Stainless steel or aluminum. Pestles and grinding vessels of the same size can be used interchangeably and all components can be autoclaved.

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Size	A	B	C
Capacity of grinding chamber without pestle, ml	10	30	35
Overall length of pestle, mm	215	230	235
Each	9.05	12.65	17.75

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NOTE—Can be furnished with Aluminum pestle rod at .22 less in price.



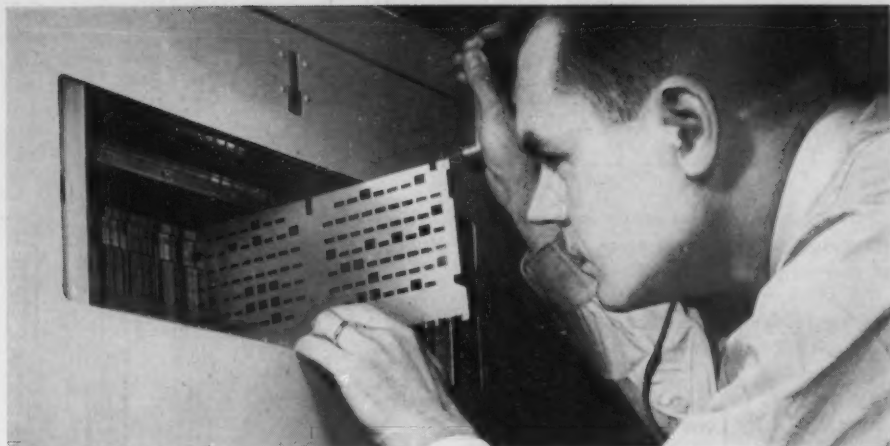
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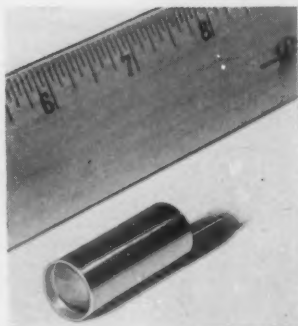
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